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Volume 234 JANUARY 31, 1946 Number 5

A TICK-BORNE EPIDEMIC OF TULAREMIA

LIEUTENANT COLONEL WILLARD B. WARRING, M.C., A.U.S., AND
MAJOR J. STERLING RUFFIN, JR., M.C., A.U.S.

BECAUSE tularemia has been generally regarded as a relatively infrequent disease, and because emphasis has been placed on its transmission by contact with animals, especially rabbits, an epidemic of 50 cases most of which were caused by tick bites is reported. These cases occurred among soldiers in the Tennessee maneuver area from March to December, 1943. Grouped according to the Hughes[1] classification of tularemia, these cases were divided as follows: ulceroglandular type, 35 cases; pulmonic type, 11 cases; glandular type, 3 cases; mixed ulceroglandular and pulmonic type, 1 case. All patients but 1 recovered.

Tularemia has been reported in every state of the Union except Vermont.[2] *Pasteurella tularensis* has been found in over twenty kinds of wild life.[3] Ticks, deer flies and cottontail rabbits are the three greatest sources of infection for man.[4] Transference of the disease between human beings has been reported.[5]

Although transmission of *P. tularensis* by several varieties of ticks has been demonstrated,[3, 6, 7] a survey of the area in which the present cases arose

TABLE 1. *Incidence of Contact.*

NATURE OF CONTACT	NO. OF CASES	PERCENTAGE
Tick bite	32	64
Rabbit	5	10
Unknown, probably contact with tick	13	26
Total	50	

revealed that all specimens were *Amblyomma americanum*, the so-called "lone-star tick."[8, 9] Parker[10] was unable to demonstrate *P. tularensis* from these ticks by culture, but previous studies in his laboratory had shown that the nymphs and larvae of *A. americanum* of the same generation transmitted *P. tularensis*.[11]

A definite history of tick bite prior to onset of illness was obtained in 32 of the 50 cases in this series (Table 1). Five appeared to be due to direct contact with rabbits. In 13 cases, a history of tick bite could not be obtained. Since these soldiers were bivouacked in an area highly infested with ticks, and since *P. tularensis* can penetrate the unbroken skin,[12] it seems justifiable to assume that the ticks were the transmitting agents.

The onset of symptoms in the proved cases of tick bite occurred within one to twenty-one days. In 50 per cent of all cases the onset was acute. The outstanding symptoms were generalized aching, especially marked in the lumbosacral region and the lower extremities, headache, shaking chills, debilitating sweats, pain and tenderness in the regional lymph nodes, unproductive cough, weakness, dizziness, nausea, vomiting, anorexia and abdominal pain. In 5 cases, abdominal pain and tenderness, together with spasm of the abdominal muscles,

TABLE 2. *Site of Primary Lesion.*

SITE	NO. OF CASES	PERCENTAGE
Arm, including hand	13	26
Upper two thirds of thigh and perineum	8	16
Lower abdomen	7	14
Leg, including foot	7	14
Buttocks	2	4
Scapular region	2	4
Buttocks region	2	4
Upper anterior chest wall	1	2
Unknown	8	16
Total	50	

suggested some acute disorder within the abdomen. Severe prostration was the rule. In 6 severely ill patients, marked delirium followed by drowsiness was present, the former being most marked in the pulmonic type of disease, which was also characterized by chest pain, unproductive cough and dyspnea out of proportion to the physical findings.

At the site of infection or bite were punched-out ulcers varying from 0.5 to 3 cm. in diameter. The edges were raised, irregular and surrounded by induration and erythema. The primary ulcers were found on the upper and lower extremities, perineum, buttocks, lower abdomen and scapular region (Table 2). In the majority of cases there was only one ulcer.

Enlarged regional lymph nodes, single or multiple, and varying from 2.5 to 6 cm. in diameter were found in every case with an obvious primary lesion and in 3 without one. The nodes were at first nontender, but as they increased in size they became tender and fluctuant and the overlying skin became reddish purple and thin. If not incised, these nodes usually suppurated and drained. In 38 cases with nodular involvement, the nodes were suppurative in 35 and nonsuppurative in 3. In 6 cases, nodes in other areas enlarged simultaneously with regional nodes draining the affected area; they slowly resolved without softening.

In 8 cases, a diffuse, erythematous, maculopapular eruption, distributed over the entire body but most pronounced over the extremities, appeared between the fifth and eleventh days of the disease. In 2 cases, it was morbilliform. The average duration of the eruption was eight days.

Two cases with acute fibrinous pleurisy and 3 with pleural effusion were encountered in the ulceroglandular type. In the pulmonic type, findings consistent with pneumonia were present. In the more serious of these cases, there appeared definite areas of consolidation involving one or several lobes, accompanied by cyanosis and dyspnea. Resolution of the pneumonia began in the third week and was extremely slow, requiring from five weeks to six months for completion.

Between the second and the fourth week, pleural effusion occurred in 9 of the 11 patients with pure pulmonic involvement. After repeated thoracenteses, the effusion subsided in ten days to five months, with an average of seventy-five days. The fluid was either greenish or serosanguineous, its specific gravity varied from 1.015 to 1.022 and the predominating cells were lymphocytes. Direct smears showed no organisms.

In 1 case, severe dyspnea was caused by a mass in the mediastinum, which gradually increased in size. The patient died on the tenth day of illness, and at autopsy the mediastinum was filled with enlarged lymph nodes.

In early stages of the disease, fever was continuous, varying between 101 and 105°F. Later there were morning remissions, and in the majority of cases the fever fell by lysis to normal in the fourth week of the disease. In patients with pleural effusion, thoracentesis caused a drop in temperature and a decrease in respiratory embarrassment.

The primary skin lesion healed with scar formation in four to seven weeks.

The patient's reaction varied from mild constitutional symptoms to marked prostration, depending on the severity of the disease. Convalescence was slow. Weakness, lassitude and loss of weight persisted for an indefinite period of time. Most of the patients have been in the hospital for three to six months and are still convalescing.

There was nothing significant in the white-cell counts, since they varied from normal to 15,150. The differential count revealed a slight shift to the left.

In all 50 cases, diagnosis was confirmed by agglutination tests which were positive in dilutions of serum varying from 1:320 to 1:10,240. The agglutinins were usually present in the second or third week of the disease, and the highest titers were reached between the third and the eighth week — a fact that is of diagnostic significance. Cross agglutination occurred in 5 cases with *Brucella abortus* and in 1 case with Proteus OX 19. All were excluded by the laboratory procedure in which a tularemic serum agglutinates a suspension of *P. tularensis* more rapidly and to a higher titer than it does *Br. abortus*, *Br. melitensis* or Proteus OX 19 antigens.[3]

Cultures made from the pleural exudate on the usual laboratory mediums to exclude the presence of pathogenic bacteria were negative. Smears of material from the ulcers, suppurating nodes and sputum revealed no *P. tularensis*. Guinea pigs were inoculated but unfortunately died of some other infection that became epidemic in the animal house.

The treatment was nonspecific and supportive. Oxygen given early to patients with pneumonia and continued throughout the acute stage seemed to offer the best chance for recovery. Wet dressings and bland ointments were applied to ulcerated lesions. When softening of regional nodes occurred, surgical incision and drainage were instituted. Thoracentesis performed in cases with pleural effusion caused an amelioration of symptoms. Administration of sulfathiazole and sulfadiazine was without apparent benefit.

Diseases with which tularemia may be readily confused include sporotrichosis, actinomycosis, meningitis, typhoid fever, Rocky Mountain spotted fever, acute infectious mononucleosis, lymphogranuloma inguinale, typhus fever, pneumonia, measles, tuberculosis, malaria and undulant fever.

The laboratory methods of confirming the diagnosis are three in number — growth of the organism from the blood or pleural or spinal fluid on a blood cysteine agar medium, inoculation of guinea pigs with this material and repeated serum agglutination tests.[6] The agglutination test is regarded as one of the most reliable confirmatory tests in the field of serology.[3] Ransmeier and Ewing[13] have shown that a positive tularemic agglutination titer may persist for a number of years. We have had no experience with Foshay's[14] intradermal test.

The following cases are representative of the various types of tularemia that were encountered.

Case Reports

Ulceroglandular Type

Case 1. A 22-year-old officer was admitted to the hospital complaining of generalized aching, chills and fever. The

previous day he had removed from his right thigh a tick that had been present for an unknown period of time.

Physical examination revealed an acutely ill man with a small punched-out ulcer on the anterior aspect of the right upper thigh and enlarged, smooth, discrete lymph nodes measuring between 2 and 4 cm. in diameter in the right inguinal region.

Fever varying between 101.8 and 104°F. continued for 12 days, after which remissions occurred for 6 days, with a gradual decline by lysis to normal levels. The white-cell count varied from 6250 to 11,400. Repeated dark-field examination of material from the ulcer, the Frei test, the Kahn test and urinalyses were all negative. Culture from the ulcer showed a nonhemolytic *Staphylococcus albus*. The serum agglutination titer for tularemia on the 20th day was 1:10,240.

Convalescence was uneventful. At the end of 30 days the ulcer had healed and the inguinal nodes were nontender, although still enlarged. The patient was discharged to duty complaining of slight weakness.

Case 2. A 30-year-old soldier was admitted to an evacuation hospital on May 28, 1943, complaining of generalized aching, headache, fever, chills, sweats, backache and slight stiffness of the neck. Two days previously a tick had been removed from the right arm. Physical examination was negative except for a temperature of 100°F.

On June 7, the patient was transferred to a station hospital because of fever of undetermined origin. He was acutely ill, and his previous symptoms had become exaggerated. Moreover, the patient presented signs of cerebral irritation, which was manifested by restlessness, irritability and mental confusion. The temperature on this admission was 105.4°F. Physical examination showed a small punched-out ulcer on the right forearm just distal to the elbow, enlarged, tender lymph nodes in the right axillary region, slight nuchal rigidity and abdominal distention. The white-cell count was 13,000. The results of spinal-fluid examination were within normal limits. An agglutination test for tularemia on blood taken at the time of admission was negative. On June 8, a discrete, red, macular rash appeared on the trunk and arms. The abdominal distention became more marked, and the patient vomited moderate amounts of a coffee-colored material and became stuporous. For 8 days there was continuous fever ranging between 103 and 105°F., but on the 14th day the temperature began to drop by lysis and symptoms gradually subsided. On June 15, the agglutination titer for tularemia was 1:1280.

On July 29, the patient was transferred to another station hospital and thence to a general hospital and finally to another general hospital. During this interim the ulcer had healed, but the right axillary nodes had become more enlarged and had gradually softened. A thick, greenish exudate was removed from these nodes by aspiration on several occasions.

At the latter general hospital, 3300 units of penicilllin was injected into one of the abscess cavities after aspiration, but this appeared to make the abscess worse. By October 11, the abscess had healed. The agglutination titer on August 27 was 1:1282. Because of weakness, the patient remained in bed until October 27. Later he was placed in a group participating in a reconditioning program. The total hospitalization period was 203 days.

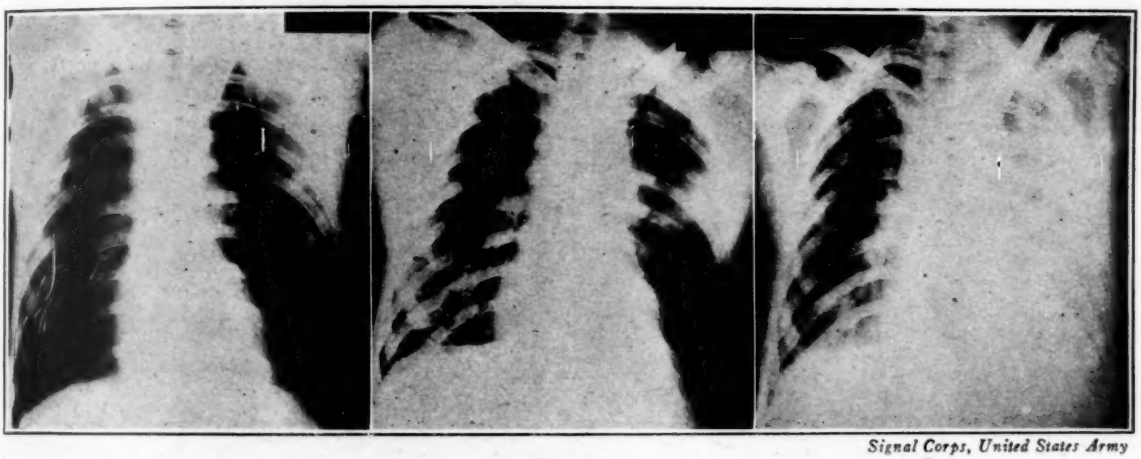
Mixed Ulceroglandular and Pulmonic Type

Case 3. A 24-year-old soldier was admitted on June 18, 1943, complaining of generalized aching, headache, malaise, fever, sweating, colicky abdominal pain, and diarrhea of 2 days' duration. He had removed ticks from his body on several occasions during the previous 2 weeks.

Physical examination revealed an acutely ill, oriented patient with a temperature of 103.6°F. and marked tenderness over the right costovertebral angle. The white-cell count was 10,700. The urine gave a +++ test for albumin.

On July 21, an unproductive cough and pain on inspiration developed in the lower right chest. The patient appeared critically ill and was cyanotic and dyspneic. Physical examination and x-ray examination of the chest revealed signs of consolidation in the right lower lobe and a widened mediastinum (Fig. 1*B*). The pneumonic process rapidly progressed until it involved almost all the left lung and the middle and lower lobes of the right lung. A pleural effusion developed in the left side of the chest (Fig. 1*C*). The spleen was palpated 2 fingerbreadths below the left costal margin. The temperature varied between 101.2 and 105.4°F. The patient became delirious, and the prostration, dyspnea, and cyanosis increased. Blood, stool and urine cultures were negative. Repeated sputum examinations were negative for acid-fast bacilli. On the 6th day of the disease, the white-cell count was 6750 and remained at this level until the death, which occurred on the 10th day.

Autopsy. The significant post-mortem findings were as follows. The left chest contained 1000 cc. of cloudy, straw-colored fluid, in which were flecks of yellow fibrinous material. Findings consistent with pneumonia were present in the entire left lung and the lower lobe of the right lung. In addition, in the left upper lobe there were many indurated areas, which



Signal Corps, United States Army

A B C

Figure 1. *Case 3.*

The interpretations of these bedside x-ray films were as follows: A (*7–19–43*) "*There is hilar adenopathy on the left. The lung fields are too dark to reveal any interstitial changes*"; B (*7–21–43*) "*There is a considerable amount of peribronchial infiltration in the right base. There is a small area of consolidation in the region of the third interspace on the left. The mediastinum appears to be widened and irregular*"; C (*7–24–43*) "*There is a massive pleural effusion involving the left chest, but lung markings are seen in the upper third. The hilar adenopathy appears to be practically the same as that in the previous films. The infiltration in the right base has slightly cleared. The mediastinum is widened.*"

were nodular in form and consisted of necrosis and caseation. The nodules varied from 1.5 to 3.0 cm. in diameter. The mediastinum contained large masses of purple-black, firm, enlarged lymph nodes, varying from 1.5 to 4.0 cm. in diameter. They were anterior to the esophagus and extended to the hilar region of each lung. All showed areas of necrosis and caseation. All the viscera, including the brain, showed moderate congestion. Both the spleen and the liver were markedly enlarged. The spleen showed necrosis and cell fragmentation, and the liver contained areas of abscess formation. Blood taken from the heart revealed a positive tularemic agglutination titer of 1:320.

Pulmonic Type

CASE 4. A 23-year-old officer was admitted on October 9, 1943, complaining of generalized aching, chills, fever and unproductive cough. During the previous 10 days he had been bitten by many unidentified insects. Since he had been billeted in a tick-infested area, it seemed probable that some of the bites had been by ticks.

Physical examination revealed a prostrated man with a temperature of 103°F., multiple insect bites over the entire trunk and extremities, consolidation of the upper lobe of the left lung and moist rales over the lower lobe of the right lung. A roentgenogram of the thorax showed a diffuse infiltration in the upper left lobe (Fig. 2*A*).

On the 5th day, the temperature was 99.4°F., and it continued intermittently at this level for 7½ months. The blood agglutination titer for tularemia was 1:2560 on November 6 and 1:640 on January 7, 1944. After 225 days of hospitalization, the patient still complained of weakness, malaise and slight discomfort in the left upper chest. Serial roentgenograms revealed a gradual clearing of the pneumonic process in the left upper lobe. At the end of 7½ months, however, it was still undetermined whether this area represented a continued infiltrative process or fibrotic changes (Fig. 2*C*).

SUMMARY

Ticks are important carriers of *Pasteurella tularensis*. Enlargement of regional lymph nodes seems to be characteristic of the disease, especially in cases with a definite primary lesion. Convalescence is prolonged. The agglutination test is considered the most reliable diagnostic test for tularemia.

Some representative cases of the various types of tularemia encountered in this series of 50 cases are reported.

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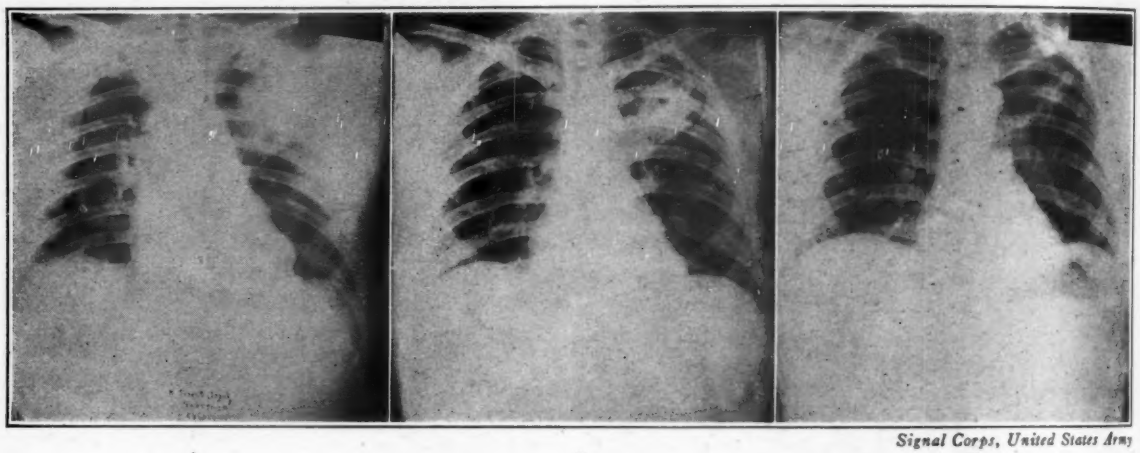

Signal Corps, United States Army

A B C

FIGURE 2. *Case 4.*

The interpretations of these x-ray films were as follows: A (*10–12–43*) "*There is an area of consolidation in the left upper lobe in the region of the second and third interspaces that resembles a lobar pneumonia*" (*this film was made in a field hospital with field equipment at a distance less than 72 inches, which explains the distortion of the cardiac shadow*); B (*10–17–43*) "*There remains a considerable amount of infiltration in the same area, with a small area of decreased density lying just above the end of the second rib, which appears to be cavitation*"; C (*2–7–44*) "*The lung fields have almost cleared. Only a small fibrotic area at the end of the second rib remains.*"

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PENICILLIN IN THE TREATMENT OF BRONCHIECTASIS*

A Preliminary Report

I. D. Bobrowitz, M.D.,† James S. Edlin, M.D.,‡ Sydney Bassin, M.D.,§ and J. Stanley Woolley, M.D.¶

OTISVILLE, NEW YORK

REPORTS on the use of penicillin in the treatment of pleural and pulmonary suppurative conditions are appearing in increasing numbers. A favorable response has been achieved in acute pneumonitis[1–4] and pulmonary abscess.[2, 3] The best effects have been obtained in infections caused by streptococci, staphylococci, pneumococci and actinomyces, and the poorest in those with mixed anaerobic bacteria. These cases were treated by intravenous or intramuscular administration of the drug. Penicillin has also been utilized satisfactorily in hemothorax to prevent infection.[2, 5] Acute pyogenic empyemas have been cleared of organisms and the toxemia prevented or reduced[2, 4–6] by aspiration of chest fluid and the intrapleural instillation of penicillin. Mixed-infection empyemas have been similarly treated[2, 5] to prepare patients for thoracoplasty.

White et al.[7] used penicillin in the prevention of postoperative empyema following lung resection. Forty-one patients had pneumonectomy or lobectomy for bronchiectasis, lung abscess, tuberculosis or neoplasm. Twenty-one of them received 150,000 units of penicillin daily — 12,500 units intramuscularly every two hours — for one week preoperatively and for two weeks postoperatively, and 20 patients served as controls. None of the penicillin-treated patients developed empyema, whereas 12 or 60 per cent of the controls did so. Penicillin was given to 12 patients with lung resection for bronchiectasis and multiple lung abscesses. Five of them had a reduction in sputum volume before operation, and 2 had a thinning and decrease in purulence of sputum. In 6 cases, penicillin given in experimental cases for seven days before operation caused hemolytic streptococci to disappear from the sputum soon after therapy was instituted. Pneumococci and streptococci were usually unaffected, although in an occasional case these organisms disappeared. Gram-negative bacilli frequently occurred and often persisted throughout the period of hospitalization. The bronchial secretions of 2 patients were tested for the presence of penicillin, and none was detectable in either. Blood samples revealed varying concentrations of penicillin. These authors believe that the preoperative administration of penicillin serves to control acute and chronic infection in the pulmonary tissues. This reduces the possibilities of postoperative infections and affords a maximum drug effect at the time the pleural space is exposed to bronchial contamination.

* * *

The present study was made to determine the value of penicillin in the treatment of bronchiectasis. Various modes of administration were utilized — intramuscular, intratracheal or intrabronchial and inhalation (nebulization) and combinations of these methods. It was particularly planned to estimate the advantages of the topical or bronchial effect of the drug.

The treatment was given to 12 patients — 10 men and 2 women — 2 of whom were Negroes. The ages varied from sixteen to thirty years. Therapy was initiated in the first case on August 9, 1944 and in the last one on April 18, 1945. The first nine patients were treated at the Municipal Sanatorium, Otisville, New York, and the last three at St. Clare's Hospital, New York City. All patients followed up were seen at the St. Clare Clinic.

Plan of Study

For a few days to a week or more prior to penicillin administration and throughout the hospitalization period, the patients were kept on postural drainage — two or three times a day for ten to fifteen minutes. When the penicillin was administered intratracheally, postural drainage immediately preceded the treatment to improve the topical action of the drug. This procedure also facilitated the collection of the sputum and assured a satisfactory total daily output. The patients were instructed to continue postural drainage after discharge.

The sputum was examined frequently and often daily before, during and after treatment, the twenty-four-hour amount being carefully determined either by measure or by weight, and the presence or absence of odor was noted. A gram-stained smear was made of each specimen received, — in twenty-four-hour collections, — and the presence and relative number and kinds of organisms were noted. A Fontana-stained smear was examined for each of the Otisville patients. Sputum cultures were done from time to time.

The sputum in established bronchiectasis usually exhibits a highly diversified flora that includes gram-positive and gram-negative organisms. Since the

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¶Director of laboratory, Municipal Sanatorium.

action of the penicillin is exerted chiefly on the former, their presence or absence in the smear constituted a practical index of the effectiveness of the penicillin, the reliability of which was borne out by the occasional cultures. In 8 patients, bioassays of the penicillin content of the sputum, urine and blood were frequently done — in some cases daily — during and after the administration of the drug and were continued until it disappeared from the specimens. The method described by Woolley and Schmidt,[8] an adaptation of the Fleming agar-hole method, was employed. With this procedure, contaminated material can be readily assayed and blood serums measured. Although the sensitivity of the test organism (*Staphylococcus aureus "H"*) employed in this method is insufficient to determine accurately amounts less than 0.2 units per cubic centimeter, the method was considered adequate because penicillin in lower concentrations is ineffective against some organisms — staphylococci and so forth. From necessity, containers for sputum and urine were kept refrigerated at all times in ice buckets near the patients' beds so that as little of the penicillin effect as possible would be lost. The amount of active penicillin per cubic centimeter for each specimen was determined, and from this the twenty-four-hour elimination was estimated.

Table 1. *Dosage and Method of Treatment.*

Case No.	Method of Administration	Duration of Treatment	Dosage	Total Dosage
		days		*units*
1	Intramuscular and intratracheal injection	12	100,000 units a day: 80,000 intramuscularly (10,000 every 3 hours) and 20,000 intratracheally	1,200,000
3	Intramuscular injection	5½	100,000 units a day: alternating 10,000 and 15,000 every 3 hr.	550,000
2	Intratracheal injection	10	100,000 units a day: 50,000 twice daily	1,000,000
4	Intratracheal injection	4	250,000 units a day: 100,000 in morning, 150,000 in afternoon	1,000,000
5	Intratracheal injection	4	250,000 units a day: 100,000 in morning, 150,000 in afternoon	1,000,000
6	Intratracheal injection	4	250,000 units a day: 100,000 in morning, 150,000 in afternoon	1,000,000
7	Intratracheal injection	30	50,000 units a day	1,500,000
8	Inhalation	30	50,000 units a day: 10,000 every 3 hours for five doses	1,500,000
9	Inhalation	60	100,000 units a day for first 20 days: 20,000 every 3 hours for 5 doses; then 50,000 units a day for 40 days: 10,000 every 3 hours for five doses.	4,000,000
10*	Intratracheal injection and inhalation	105	100,000 units a day intratracheally for 10 days; then 100,000 units three times a week by inhalation (100,000-unit doses) for 95 days.	4,900,000*
11*	Intratracheal injection and inhalation	115	100,000 units a day intratracheally for 10 days; then 100,000 units three times a week by inhalation (100,000-unit doses) for 105 days.	5,500,000*
12*	Inhalation	60	100,000 units a day for 10 days; then 100,000 units three times a week.	3,100,000*

*Patient still under treatment.

Results

The diagnosis was made in every case by means of a bronchogram with lipiodol. The bronchiectasis was multilobar in all 12 cases and bilateral in 11. Two lobes were involved in 4 cases, three in 7, and four in 1. In other words, the 12 patients had thirty-three bronchiectatic lobes. The left lower lobe was involved in 12 cases, the right lower lobe in 9, and the right middle lobe and lingula portion of the left upper lobe in 6 each. Of the thirty-three bronchiectatic lobes, a marked saccular condition was present in nineteen, a moderate saccular involvement in three, moderate cylindrical and varicose dilatations in six, and slight cylindrical enlargement in five. In addition, bronchiectasis existed in two lobes that were atelectatic.

The onset of symptoms followed pneumonia in 10 cases, pertussis in 1 and influenza in 1. The symptoms had existed for four to twenty-four years, with a duration of more than ten years in all but 2 cases. In 7 cases, pneumonic episodes had recurred, and in 2 of these they had done so two and three times, respectively; only 1 patient had a coexistent tuberculosis, and in this case it had been present in both upper lobes for six years.

The symptoms and physical findings were those characteristic of this condition. In addition, 2 cases gave radiographic evidence of sinus involvement.

The sputum showed varying degrees of purulence. In all but 2 cases it had a foul odor and in most cases it separated on standing into the characteristic three layers. All the specimens exhibited a more or less similar bacterial flora. The more putrid they were, the greater were the number of organisms. Gram-positive organisms predominated in all smears: chains (streptococci) were present in 9 patients, grape-like clusters (staphylococci) in 8, diplococci in 8 and rods in 2. The gram-negative organisms included fusiform bacilli in 5 patients, biscuit-shaped diplococci (*Micrococcus catarrhalis*) in 4, rods in 3, cocci in 2, and diplococci in 1. No spirochetes were found with the Fontana stain. The sputum cultures verified the findings of the sputum

smears. Anaerobic cultures revealed little of significance.

The dosage of penicillin and the methods of administration are shown in Table 1. The intramuscular doses were given in a concentration of 5000 units per cubic centimeter of physiologic saline solution. In all the intratracheal cases except Case 7, the penicillin was administered by the supraglottic method, preceded by topical cocainization. In Case 7, an intrabronchial catheter was used for three days and an intratracheal catheter for nine days, but otherwise the usual supraglottic route was utilized. During all these intratracheal instillations the patient was placed so that the drug could reach the affected lobes. Each dose was dissolved in 10 to 20 cc. of saline solution. The inhalation method consisted in nebulization of the penicillin solution in a vaporizer. The technic employed was that previously described.[9] In the Otisville cases, however, a glass Y connection was placed on the tube leading from the oxygen tank to the vaporizer and controlled by the patient's closing or opening the open end with his finger. When the connection was open, the oxygen passed through the Y tube to the outside and not to the nebulizer and the patient was able to rest. When it was closed, the oxygen passed to the vaporizer, forming a penicillin mist or vapor, which was inhaled. An L-shaped glass extension was also connected to the stem of the vaporizer, which dipped down behind the base of the tongue so that the penicillin spray could be directed toward the larynx. Each dose was dissolved in 2 to 4 cc. of saline solution.

There were no real difficulties in administering the drug. Three of the patients receiving intratracheal administration (Cases 4, 5 and 6) experienced slight nervousness and sleeplessness as the result of the cocainizations. Use of the intrabronchial catheter was soon discontinued, since it appeared to be irritating. In 1 patient (Case 8) treated with inhalation therapy, a dermatitis occurred on the face and lips. This was relieved by a vaseline ointment without discontinuation of therapy. A skin test and a patch test with penicillin were both negative.

Of the 10 patients with a foul sputum, in 9 the odor completely cleared and in 1 it slightly diminished. The former effect was achieved within one day in 4 patients — intratracheal administration in 2, inhalation in 1 and intramuscular and intratracheal administration in 1; within forty-eight hours in 3 cases — intramuscular administration, intratracheal injection, and intratracheal injection and inhalation, each in 1; and after intervals of three and six days the 2 other cases — (inhalation in 1 and intratracheal administration and inhalation in 1). Whenever the offensive smell of the sputum disappeared after penicillin, the effect continued throughout the period of therapy. In 3 cases the treatment is still being continued. The odor returned following discontinuation of penicillin in 3 patients after intervals of three days, four days and three months, respectively. Two patients had no recurrence of odor, but the followup lasted for only eight days in one and one month in the other. Sufficient time has not elapsed to determine the lasting effect of the drug in these cases. One patient left the hospital against advice, and there is no information on the present status of his sputum.

TABLE 2. *Changes in Amount of Sputum after Penicillin Therapy.*

CASE NO.	METHOD OF ADMINISTRATION	BEFORE PENICILLIN	AFTER PENICILLIN		SPUTUM LEVEL AFTER CESSATION OF TREATMENT
		AMOUNT	AMOUNT	RAPIDITY OF EFFECT	
1	Intramuscular and intratracheal injection	180-240 cc.	45 cc.	6 days	60 cc. (2 mo.); 120 cc. (3½ mo.).
3	Intramuscular injection	60 cc.	38 cc.	2 days	Patient left against advice
2	Intratracheal injection	45-60 cc.	22 cc.	5 days	15 cc. (3 wk.); 30 cc. (1 mo. and 3 mo.).
4	Intratracheal injection	300 cc.	90 cc.	3 days	40 cc. (1 wk.); 70 cc. (3 and 4 wk).
5	Intratracheal injection	90 cc.	40 cc.	4 days	42 cc. (6½ mo.)
6	Intratracheal injection	120 cc.	40 cc.	4 days	80 cc. (1 wk.); 55 cc. (3 wk. and 6½ mo).
7	Intratracheal injection	209 gm.	108 gm.	4 wk.	No followup
8	Inhalation	29 gm.	11 gm.	4 wk.	20 gm. (4 mo.)
9	Inhalation	145 gm.	50 gm.	4 wk.	79 gm. (8 days)
10	Intratracheal injection and inhalation	180-240 cc.	36 cc. 14 cc.	5 days 9 wk.	Treatment continued
11	Intratracheal injection and inhalation	70 cc.	23 cc. 10 cc.	4 days 6 wk	Treatment continued
12	Inhalation	110 cc.	28 cc. 12 cc.	6 days 7 wk.	Treatment continued

The changes in the sputum volume are shown in Table 2. The figures covering the penicillin effect on the total twenty-four-hour sputum amount represent the lowest sputum level that was steadily maintained and the time during the period of treatment at which it occurred. Actually there was a progressive diminution in sputum output, which started as soon as treatment was begun, but the maximum reduction took place at variable periods after the treatment was initiated. As indicated by the table, this required from a few days to several weeks. The patients treated by intratracheal instillation in all cases but 1 showed the maximum effect within a few days. The inhalation cases and those with combined intratracheal injection and inhalation treatment showed a significant early reduction, but the most marked diminution required several weeks. In every patient but the one who left against advice, the sputum reduction was at least 50 per cent. For

the entire group, excluding those still under treatment, the average was 63 per cent. It is possible that the postural drainage itself accounted for some diminution in sputum. The best effect has thus far been shown in patients receiving combined intratracheal injection and inhalation therapy. In the patients followed up for periods averaging over three months, however, cases with an increase in sputum output occurred after treatment was discontinued. In 2 of the cases with intratracheal administration, the sputum continued to diminish for a short time (one to three weeks) before it increased. In no case did it return to its original level present before therapy, and usually it continued at only half of the pretreatment amount. Since postural drainage and the collection of sputum cannot be so well controlled after discharge from the institution, the expectoration may have been greater than that reported by the patients.

As would be expected, the penicillin tended to clear the sputum of organisms, especially the gram-positive ones, with rapidity. As a result of this, the pus cells were materially reduced. In 7 cases, all gram-positive organisms disappeared completely from the sputum. This was achieved by every method of administration, except in the patient given penicillin intramuscularly who left against advice. In the intratracheally treated cases, this effect occurred within two or three days, whereas in those treated by inhalation it required a week or two. In 3 patients, the gram-positive bacteria were eliminated within one or two weeks, but a few reappeared while treatment was continued. In 2 cases, including that of the patient incompletely treated, occasional gram-positive organisms remained.

Gram-negative organisms were also favorably influenced by the treatment. In 4 cases, — 3 treated intratracheally and 1 by inhalation, — they disappeared. With the intratracheal injection, this occurred within two to four days, and with inhalation at the end of two weeks. In the other cases a rare or occasional number of gram-negative organisms persisted.

In every case there was a decrease in the purulence of the sputum, and usually only a few cells remained. As with the bacterial changes, the intratracheal injection produced the maximum effect in a few days, and inhalation technic in one or two weeks.

In all patients followed up, there was a rapid change in the bacterial content and purulence of the sputum as soon as the penicillin was discontinued. In 5 of the 8 patients with a completed course of treatment, gram-positive organisms appeared or increased within two to five days after the penicillin was stopped and continued to multiply. In 3 cases, — all treated intratracheally, — the organisms appeared or increased after an interval of one or two weeks and later became more numerous. In 6 patients, gram-negative organisms reappeared or increased, either in a few days or a few weeks.

In every case the sputum also became more purulent when the penicillin was stopped. This took place either within a few days or after a week or two.

There was symptomatic improvement in every patient. Cough was rapidly alleviated, and in all but 2 patients the effect became evident within a few days. The cough decreased to the point where expectoration took place with postural drainage only. Night coughing almost ceased, and the stimulation to cough formerly caused by exertion, laughter, deep breathing or change in position no longer occurred. Dyspnea was much reduced, and in 1 patient it was eliminated. Wheezing and chest heaviness were also relieved. Anorexia was improved. Six patients gained weight while under treatment, and 4 of these continued to do so after penicillin was discontinued. Significantly, several of these patients had been markedly under weight for many years. Two of the patients began to gain after treatment. A slight loss of weight occurred in 3 patients, 2 of whom had had a normal weight before admission. One patient showed a marked reduction in nasal discharge. Incidentally, in 1 case with a pustular acne of the face the condition entirely cleared with treatment, although the skin lesions reappeared after penicillin was discontinued. The 1 patient who had tuberculosis and bronchiectasis had blood-streaked sputum for two days in the first week of treatment, expectorated about 15 cc. of blood twelve days after penicillin was initiated and also had blood-streaked sputum for several days during the third week of treatment; he had, however, had similar symptoms before — severe hemoptysis on two occasions one year previously, with streaking over a period of three or four weeks. There has not been a sufficiently long follow-up period to determine the duration of the symptomatic benefits. It was noted, however, that cough and expectoration again increased but that the general well-being continued after cessation of therapy.

In 7 patients, there was a change in physical signs, with the chest appearing clearer, owing to a decrease in the amount of moisture. The white-cell counts and sedimentation rates revealed no significant changes during treatment, except in 1 case, in which a marked diminution in leukocytosis occurred.

The assay studies revealed the following results. With intramuscular penicillin (Case 3), only once was the drug found in the sputum. This was on the first full day of treatment, and the assay showed 0.4 units per cubic centimeter. That there was good systemic absorption was indicated by blood levels of 0.2, 0.3 and 0.4 units per cubic centimeter and the presence of considerable penicillin in the urine. The lack of penicillin in the sputum of patients receiving intramuscular treatments was also found by White et al.[7]

The first patient treated intratracheally alone (Case 2) received 1,000,000 units in ten days. A very high penicillin titer was found in the sputum, with an average of 284 units per cubic centimeter, which assured an excellent topical or bronchial effect. The penicillin was given in a selective manner by instillation in the diseased lobes. That excellent pulmonary absorption occurred was indicated by the high blood and urine levels, with probable good parenchymal effect. The urine concentration averaged 38 units per cubic centimeter, which meant that over 30 per cent of the total dose given was recovered in the urine. The blood levels were 0.4, 0.5 and 0.6 units per cubic centimeter. Penicillin was recovered from the sputum for eight days and from the urine for three days after treatment was discontinued.

The next three intratracheally treated patients (Cases 4, 5, and 6) received 1,000,000 units in four days. Extremely high concentrations of penicillin were found in the sputums, with an average of 831, 552 and 159 units per cubic centimeter, respectively. The low level in the last patient was due to the fact that the administration of the drug was somewhat difficult and that not all of it reached the lung. The urine concentration averaged 38, 19 and 36 units per cubic centimeter, respectively. In 2 cases the blood level did not rise above 0.1 units per cubic centimeter, and in 1 case it reached 0.25 and 0.45 units. In these patients penicillin was found in the sputum for no longer than 3 days and in the urine for no longer than two days after treatment was stopped.

Although an extremely high sputum concentration of penicillin was obtained for a short time, this method of rapid intensive administration had several significant disadvantages. A penicillin concentration in the sputum beyond an optimum level, or one adequate to control the bronchial and parenchymal infection, is undesirable because the excess penicillin is lost in the expectoration. The amount of penicillin absorbed through the lung is indicated by the concentration in the urine and blood. The penicillin levels in the urine and blood of these 3 patients were lower than that found in the patient given the same dose over a period of ten days instead of four days. Penicillin was also found for a shorter time in these patients after the treatment was stopped. Because of this, it was decided to utilize the penicillin in the form of a smaller dose and to administer it over a longer period.

The next patient (Case 7) received 50,000 units intratracheally for thirty days, a total dosage of 1,500,000 units. The assay studies revealed an average sputum concentration of 101 units per cubic centimeter, a urine level of 8.3 units and a blood concentration of 0.1 to 0.25 units. These concentrations were less than those found in the patients given penicillin intratracheally for four to ten days. The results of treatment were not so good as in the patient with ten days of therapy. The hoped-for benefit of prolongation of treatment for thirty days was apparently offset by the fact that the dosage was too small. Moreover, daily intratracheal instillations for more than a short period are definitely undesirable. It was therefore decided to use penicillin by inhalation, since this is an extremely simple method of administration. Our[9] previous experience with nebulization had indicated that drugs so given penetrate the lung, provide a topical effect and diffuse into the blood stream.

The first patient treated by inhalation (Case 8) received 1,500,000 units in thirty days (50,000 units daily). The penicillin concentration in the sputum was quite low and, although it varied greatly, averaged only 13 units per cubic centimeter — a lower concentration than that in any of the other patients except the one given intramuscular injections. The urine concentration, 1.8 units, was also the lowest in any patient. Assay of the blood showed no penicillin present on three occasions and 0.1 and 0.2 units per cubic centimeter at two other times. These low concentrations indicate that not all the penicillin vaporized enters the lungs. A certain portion reaches the buccal mucosa, pharynx and esophagus and is swallowed with the saliva. Yet with the concentration of penicillin noted in this case, a good clinical and bacteriologic effect was evident.

It was decided that a larger dose was needed to build up a higher concentration in the bronchi and that the administration should be continued for a longer period of time. The next patient treated by inhalation (Case 9) received 4,000,000 units in sixty days. The penicillin concentration in the sputum varied greatly but was maintained at a fairly high average level (86 units per cubic centimeter). This proved that inhalation in proper dosage could result in a favorable topical effect in the bronchi. The urine concentration averaged only 2 units per cubic centimeter, however, and three blood specimens failed to reveal any penicillin. These figures when compared with those in the intratracheal injection cases show that with inhalation there was much less bronchial and pulmonary absorption of penicillin. No assay studies were done in the last 3 patients treated at St. Clare's Hospital.

Two patients have had no follow-up, and 3 are still being treated. Of the other 7 patients, 2 were seen a month after treatment was stopped, 1 was followed for three months, 2 were followed for three and a half to four months, and 2 were followed for six and a half months.

Discussion

Boyd[10] in describing bronchiectasis states:

> There is a combination of inflammation and degradation of tissue. The wall of the bronchus is congested and

> infiltrated with chronic inflammatory cells. The mucous membrane is atrophic and the epithelium may be completely absent in places. In advanced cases, various elements of the bronchial wall, the glands, the muscle and the elastic tissue may have more or less disappeared and be replaced by dense fibrous tissue.

Hinshaw and Schmidt[11] write:

> If one reviews the pathologic picture of true bronchiectasis one sees how difficult it is for nature to repair such damage. There has been extensive destruction of irreplaceable structures in the walls of important bronchi with resultant functional impairment of the air channels and accumulation and putrefaction of secretion which lead to further destruction and greater functional impairment.

The destructive changes of bronchiectasis are irreversible but the findings in the present series point to possibilities for the control of bronchiectasis. This study has shown that extremely favorable results can be achieved in the treatment of bronchiectasis with penicillin. Although the sputum was not entirely eliminated, a great diminution in expectoration occurred. It was demonstrated that the extremely foul sputum odor could be removed, organisms practically eliminated, and purulence greatly reduced. Intratracheal penicillin produced the latter two effects within a few days, and inhalation produced them in one or a few weeks. Symptomatic improvement, invariably of considerable degree, also took place. When treatment was discontinued, expectoration increased, organisms reappeared, pus cells became more numerous, and in many cases the odor returned. The sputum level was below the original one, and much of the symptomatic improvement persisted. These findings indicate that the results of treatment can be properly judged only after a long follow-up period and not by immediate changes alone.

It is generally accepted that the only cure for bronchiectasis is lung resection. Most, if not all, of the patients in this series, however, could not be treated surgically because of multilobar and bilateral involvement, and instead received palliative or symptomatic treatment. Moreover, all but the last 3 patients had only a short temporary course of treatment.

We wish to emphasize that while the penicillin was administered and for some time thereafter, excellent results were obtained, which represent a definite accomplishment in the treatment of bronchiectasis. A method has been demonstrated that can also be used in the preoperative preparation of patients for lung resection. With the expectoration markedly diminished and the sputum free of organisms, it is believed that the bronchiectatic lung can be handled during operation with little danger of aspiration into healthy pulmonary tissue and with diminished chances of an empyema should a bronchial fistula occur.

If the subjective and objective improvements obtained by our patients while on penicillin can be indefinitely continued by prolongation of treatment, a form of therapy is available in nonsurgical cases with marked advantages not present in other nonoperative methods. This therapy requires the use of penicillin for an extremely long period, and perhaps indefinitely, somewhat in the manner that insulin must be constantly taken to control diabetes. The last 3 patients in this series are still being treated after intervals as long as sixteen weeks, and the penicillin will be continued. Because of the sustained effectiveness of continued therapy, although no cure may occur, it seems likely that the progressive and irreversible progress of the condition to chronic invalidism and death can be interrupted. Possibly the occurrence of pulmonary complications — bronchitis, pneumonia, lung abscesses and empyema — and the general consequences of bronchiectasis — amyloidosis, cardiac failure and brain abscesses — can also be reduced or prevented. The control of the bronchiectatic condition is of particular value during the winter months when pulmonary complications are rife. It is also possible under this treatment to remove the "psychic, social, economic and physical handicaps" of bronchiectasis.

Heretofore no therapy has been available that could control the bronchial and pulmonary infection of bronchiectasis. Penicillin has definitely curtailed the evidences of suppuration in our cases. It is within the range of possibility that penicillin in sufficient dosage and administered for a long enough period may eliminate the bacterial infection and abolish the expectoration and that repair may ensue. Although this program may be utopian, our findings indicate that the further use of penicillin is well justified.

Studies are now under way to determine the precise dose and length of treatment that will achieve the best results. Intramuscular injection therapy is not being employed because of the negligible amount of penicillin obtained in the bronchial secretions and the discomfort of repeated injections. The intratracheal route gives the most effective local concentration of the drug combined with a high absorption rate. For the treatment of bronchiectasis, penicillin is required over a long period, and it is not advisable to have daily intratracheal instillations or intrabronchial catheterizations for so long a time. There are the difficulty of anesthetization, the presence of sensitivity to cocaine and the possibility of reaction from manipulation with a bronchial catheter, as occurred in Case 7. A short intensive course with intratracheal instillations of at least 100,000 units daily is, however, suggested as suitable for preoperative preparation for lung resection because of bronchiectasis. This method can also provide an immediate maximum and rapid effect prior to continuation of penicillin by inhalation, as was done in Cases 10 and 11. Repeated short courses may also be of value.

Penicillin inhalation is effective, and when given in proper dosage provides an excellent bronchial concentration and parenchymal absorption. The inhalation method is, moreover, the simplest pro-

cedure of any available. There is somewhat of a loss in its administration, however, and not all the drug reaches the lungs. For a result comparable to that achieved with intratracheal instillation, much more penicillin has to be used, but the increasing availability of the drug and its lowered cost warrant the use of this method. Inhalation is not necessarily a hospital procedure and is easily applied either in the physician's office, the clinic or the patient's home. The vaporizer is extremely easy to employ with an oxygen tank or by hand, although the latter method is the more difficult of the two. Experience has shown that patients can easily be taught to utilize a vaporizer and oxygen tank at home, and this has been done in the treatment of chronic pulmonary emphysema.[12] Penicillin can be used in this manner over a long period of time, since there are no evidences of toxicity.

It is desirable to treat adequately the sinusitis that is often present in patients with bronchiectasis. This reduces the possibility of drainage of purulent material from the sinuses to the respiratory tract.

In using the treatment described on a long-term basis, one must also take into consideration the possibility that the organisms will in time show resistance to the penicillin. In 3 of our cases, a few organisms reappeared during treatment. Treatment over a much longer period is required to gain definite information on this point. Gallardo[13] studied 112 cases of traumatic wounds of the extremities and draining abscesses and determined the naturally resistant and fast strains of staphylococci, both pathogenic and nonpathogenic. Nine and four tenths per cent of these organisms acquired resistance to the penicillin, and 12.4 per cent had natural resistance. The exact period at which the organisms became fast was not known, but differences of five to forty days were noted. Gallardo considers it advisable to assay routinely the sensitivity of bacteria from infected foci in all patients in whom penicillin is contemplated or in progress. Demerec[14] studied the production of strains of staphylococcus resistant to various concentrations of penicillin, and found that such strains could be obtained by growing the bacteria on mediums containing increasingly higher concentrations of the drug. Resistance was not induced or acquired through interaction between the bacteria and the penicillin, but appeared as an inherited characteristic that originated through mutation. The development of penicillin-resistant staphylococci during therapy has been attributed to the use of sublethal concentrations of the drug and is considered of little clinical significance.[15]

This question of resistance of organisms is still an unsettled one and its relationship to therapy is yet to be determined.

Summary

A report is made of 12 cases of severe bronchiectasis treated with penicillin.

The drug was administered by intramuscular injection, intratracheal injection and inhalation and combinations of these.

The total dosage of penicillin varied from 550,000 to over 5,500,000 units, and the length of treatment from four to one hundred and fifteen days. In 3 cases, therapy is still being continued.

The concentration of penicillin in the sputum was highest with intratracheal administration, less with inhalation and lowest with intramuscular injection.

The most rapid results were achieved with intratracheal instillations.

The simplest method of administration is inhalation.

Remarkable results were achieved with treatment. The sputum was considerably diminished and its odor was removed, most organisms were eliminated, and purulence was reduced. Considerable symptomatic improvement also took place. These changes were maintained while the penicillin was continued but did not long persist when it was stopped.

As symptomatic therapy for nonoperative cases and possibly for the control of bronchiectasis, penicillin will be required over a long period of time and perhaps indefinitely.

Penicillin given intratracheally and by inhalation is also suggested as a form of preoperative preparation for lung resection for bronchiectasis.

The results justify the further investigation of the use of penicillin in the treatment of bronchiectasis.

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THE CLINICAL ASPECTS OF RHEUMATIC FEVER IN ADULTS*

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RHEUMATIC fever has been generally regarded as a disease principally affecting children, and its occurrence in adults has as a consequence been more or less ignored. The high incidence of this disease among members of the armed forces has, however, served to focus attention on its importance in older persons, particularly young adults. It is the purpose of this paper to present a composite picture of the clinical aspects of rheumatic fever as observed in a series of 1000 patients studied at a large naval hospital.

ETIOLOGY

Although the etiology of rheumatic fever remains unknown, epidemiologic studies indicate that there is a close relation between the disease and epidemics of Group A beta-hemolytic streptococcus infections. In almost all our patients, there was a recent history of an acute upper respiratory infection, such as coryza, sinusitis, pharyngitis, tonsillitis or otitis media, which occurred one to four weeks prior to the onset of rheumatic fever. In some cases, scarlet fever ushered in an attack of rheumatic fever. In 6 patients, acute polyarthritis and carditis appeared during the course of German measles, but whether these manifestations were due to the virus of that disease or were related to a previous unrecognized hemolytic streptococcus infection cannot be stated with certainty.

Exercise, fatigue and damp, rainy or cold weather were found to be provocative factors. As in many other acute infectious diseases, there was a distinct seasonal variation, with the highest admission rate from December to April, inclusive, when the disease reached epidemic proportions.

Contrary to expectations, in only 38 per cent of the patients was it possible to elicit an antecedent history of rheumatic fever, chorea, growing pains or heart trouble. In many cases there was a familial history of rheumatic fever suggesting a constitutional factor.

INCIDENCE

The ages ranged from seventeen to forty-one years, with most patients between seventeen and twenty-four. All but 5 patients were men, which may to a large measure be explained by the relatively small number of women on duty in the district from which these patients originated.

SYMPTOMS AND FINDINGS

The clinical manifestations were extremely varied. In most cases, the onset was marked by the appearance of acute arthritis, with pain, swelling, stiffness, tenderness and often redness of one or more joints. The knees, ankles, wrists, elbows and small joints of the feet were those most frequently affected, although no joints escaped involvement. These symptoms were accompanied by malaise, lassitude, fatigue, tachycardia and fever ranging from 99 to 104°F., and were followed by similar involvement of other joints. Often the initial joint involvement persisted and the other joints successively became affected. The knee joints often became greatly distended with synovial fluid. Epistaxis was not infrequent, but drenching sweats were observed only rarely.

In many patients the clinical picture was less typical than the foregoing one, and it was occasionally bizarre. In some cases only mild pain and stiffness involving a single joint were noted, tachycardia, systemic manifestations and objective findings being absent. In many such cases, when the knees, ankle or foot were affected, the symptoms were misinterpreted as the result of a coincidental fall, sprain or even weak arches and were treated by immobilization. In other cases slight redness, mild tenderness and minimal swelling were encountered.

In one group of patients the only symptoms were vague muscular pains and stiffness. In another, chills and intermittent fever were the only complaints. Lumbar backache was frequent and was often accompanied by urinary frequency and the microscopic findings of pyelonephritis.

Of particular significance is the fact that the presenting symptoms were often abdominal, consisting of pain, with anorexia, nausea and vomiting and at times with diarrhea. Diffuse abdominal tenderness, with or without the rebound phenomenon, was usually found. In some of these cases the clinical picture simulated that of acute appendicitis, but a careful history and close observation revealed joint pain, tenderness and stiffness, followed by evidence of acute carditis.

In 15 cases, the principal symptoms were precordial pain and dyspnea, with or without cyanosis. In these cases the joint manifestations were minor and were generally disregarded by the patient. Various degrees of auriculoventricular block, sometimes extending to complete heart block with ventricular rates as low as 20 per minute, were found by electrocardiographic studies.

Cerebral manifestations, when present, were mild, consisting mainly of drowsiness and stupor. Rarely, transient psychoses with delirium were observed in the acutely ill patients with high fever. Chorea was present in only 3 patients. In 5 patients with stiffness and pain in the cervical vertebras, meningitis was closely simulated.

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A perceptible increase in the size of the heart was observed in only a small number of patients while they were under observation. In most of these cases the enlargement was slight, unless complicated by acute pericarditis with effusion. Frequently, however, the first sound at the mitral area became muffled or diminished in intensity. In most cases a soft, blowing systolic murmur developed at the mitral area. In many of these patients it became audible over the entire precordium, and in some it became loud and harsh and was transmitted to the axilla. The systolic murmurs varied in intensity and degree of transmission from time to time and often disappeared when the patient was in the sitting position.

A low-pitched, rumbling, mid-diastolic murmur appeared at the mitral area in a number of patients. It usually developed after two to three months of hospitalization, but was observed as early as three weeks after admission, raising the question of a preexisting mitral lesion, notwithstanding the patient's denial of antecedent rheumatic infection. This murmur was best elicited during forced expiration with the patient lying in the left oblique position. In 5 cases, — none with aortic insufficiency, — it was transitory and disappeared within four weeks.

In the minority of cases, the aortic second sound became slurred and a soft, blowing diastolic murmur appeared at the left third and fourth interspaces near the sternum. In 8 patients, the murmur ultimately disappeared. In the others, it persisted and frequently became louder, longer in duration and more widely transmitted and was eventually associated with peripheral signs of aortic incompetency.

Signs of acute pericarditis were observed in 19 cases. It is noteworthy that only in these patients did pleurisy, with or without effusion, and pneumonia develop. In 5 cases, signs of pericardial effusion were elicited.

The spleen was slightly enlarged in 5 cases.

Skin lesions, when present, were usually those of erythema multiforme, but in some cases small ecchymotic areas were noted at the site of the affected joints, spreading to involve the other parts of the extremities. Subcutaneous nodules were not found in any patient of this series.

Rapid loss of weight, amounting to as much as 16 to 20 pounds, was almost invariably noted during the acute stage of the illness.

Electrocardiographic changes were observed in 63 per cent of the patients, often after only a few days of illness. These occurred with increasing frequency when serial electrocardiographic studies were made. The most frequent abnormality was prolongation of the auriculoventricular conduction time, the longest PR interval being 0.62 second. In a number of cases, although the PR intervals were within the range of normal (0.12 to 0.21 second), repeated electrocardiograms showed variations in excess of 0.02 second. These variations were interpreted as being significant of first-degree auriculoventricular block. They emphasize the importance of frequent electrocardiographic tracings in the same patient. All degrees of auriculoventricular block were observed, and occasionally that of the indeterminate type was seen. At times the QRS complexes were inverted and notched in Lead CF_4, and the ST segments were either elevated or depressed beyond normal in one or more leads. The T waves often became tiny, diphasic or inverted in one or more leads, especially in Lead CF_4. In the patients with physical signs of pericarditis, the T waves usually became inverted in the limb leads but the ST changes were slight. Premature systoles were frequently noted. Of the other arrhythmias, paroxysmal auricular tachycardia, auricular fibrillation and auricular flutter occurred in isolated cases. The occurrence of interference dissociation in 18 cases was of clinical interest, although of no pathological significance. This abnormality, ascribed to hyperirritability of the auriculoventricular node, occurred only during the acute stage of illness. The electrocardiographic changes were transient in almost all the cases, usually returning to normal within seven to twenty-one days but occasionally persisting for as long as five months. When right or left ventricular preponderance developed, it generally remained during the entire period of observation. It is noteworthy that the electrocardiographic abnormalities were more frequent and also more marked in the patients admitted to the hospital during the peak of the epidemic periods.

An increased sedimentation rate has generally been regarded as a constant finding in acute rheumatic fever. In the vast majority of cases our findings were in agreement with this observation, but in a small number of patients with mild joint involvement and electrocardiographic evidence of first-degree auriculoventricular block the sedimentation rate was repeatedly normal. Thus, the deduction may be drawn that a normal rate does not preclude the existence of active rheumatic fever.

The white-cell count usually showed a leukocytosis, ranging between 10,500 and 16,000. In the minority of patients, a mild hypochromic anemia was found. Albuminuria, pyuria and microscopic hematuria were frequently present on admission; they generally disappeared within several days.

Course

The course was variable, depending on the tenacity of the rheumatic infection. The great majority of patients recovered after a single bout of fever and ran a relatively benign course. In the others, either the acute stage was followed by a long period of low-grade activity or the remission was punctuated by a recrudescence of symptoms, usually subsequent to a hemolytic streptococcus infection of the upper respiratory tract. It is well recognized that the danger of disabling heart disease

lies principally in the cases that pursue one or the other of the latter courses. In this series, the paranasal sinuses were found to be the usual focus of persistent infection, the eradication of which shortened the course of the disease.

Only 5 fatalities occurred. In 3 of these cases, there was evidence of terminal uremia and autopsy revealed subacute glomerulonephritis. In the other 2, death resulted from congestive heart failure.

Diagnosis

In the typical case, when acute migratory polyarthritis is found in association with acute carditis, electrocardiographic abnormalities, leukocytosis and an increased sedimentation rate, the diagnosis of rheumatic fever may be made without equivocation. As indicated by the foregoing description, however, many patients do not present this combination of findings, and in these the diagnosis is likely to be difficult and the clinical picture confusing. Indeed, the manifestations of rheumatic fever may be so protean as to simulate those of many diseases. Hence, in patients with fever accompanied by arthralgia, muscular pains and stiffness, precordial pain and dyspnea, acute abdominal symptoms or acute pyelonephritis and in whom the diagnosis is in doubt, as well as in those with pyrexia of unknown origin, the possibility of rheumatic fever must receive consideration. It is unfortunate that there exists today no specific diagnostic test for rheumatic fever, and until such a test is forthcoming, careful and prolonged clinical observation is necessary in these cases. Errors in diagnosis may be inescapable, especially in patients with arthralgia and low-grade fever, representing the milder forms of rheumatic fever, a fact that has also been emphasized by Jones.[1] A history of antecedent rheumatic fever or chorea should be regarded as highly significant, whereas a familial history of rheumatic fever may be of some help and should receive consideration. Electrocardiographic changes, particularly prolongation of the conduction time, should be considered as strong evidence in support of rheumatic fever, but it must be recognized that they are not diagnostic and that at times other infections produce similar changes (Rosenberg[2]). The development of systolic murmurs per se cannot be regarded as of diagnostic value, inasmuch as they may appear during the course of any acute infectious disease and are usually produced by relative dilatation of the cardiac orifice, but the appearance of diastolic murmurs at the left third interspace near the sternum or at the aortic area, mid-diastolic murmurs at the mitral area — in the absence of aortic regurgitation — or signs of acute pericarditis may be considered as confirmatory. Determination of the antistreptolysin titer may be helpful, but only as an indication of a recent hemolytic streptococcus infection. In doubtful cases the absence of antistreptolysins tends to negate the diagnosis of rheumatic fever.

Of the many diseases that may resemble rheumatic fever, acute rheumatoid arthritis is the most frequent one. It may be differentiated by the persistent periarticular swelling of the small joints, resulting in deformities, a predilection for the proximal interphalangeal joints of the fingers and the usual freedom from cardiac involvement. It should be pointed out, however, that the relation between these diseases is still controversial and that they may coexist. Gonococcal arthritis may confuse the diagnosis, but the recovery of the specific organism from the joint fluid is conclusive evidence. The finding of gonococci in the genitourinary tract in a patient with a recent history of gonorrhea may also be regarded as presumptive evidence of gonococcal arthritis. On the other hand, a positive complement-fixation test has not by itself been found to be a reliable diagnostic aid. Septic arthritis and arthritis secondary to other acute infectious diseases may be suspected from the antecedent history of infection or from the concomitant disease. Undulant fever is generally associated with arthritis and may be identified by the finding of a high titer of specific agglutinins in the blood serum, by intradermal skin tests or by positive blood cultures. Serum sickness may also produce febrile reactions with acute polyarticular manifestations. On the other hand, a history of serum administration seven to ten days previously, the presence of urticaria and the absence of redness of the joints serve to differentiate the disease. The premeningeal stage of acute meningococcemia, when accompanied by acute arthritis, may resemble acute rheumatic fever. It may be distinguished by the history, the presence of a generalized petechial eruption and corroboratory bacteriologic studies. Acute gout at times masquerades as rheumatic fever. In these cases, the hyperuricemia, roentgenographic findings in the bones and a prompt response to colchicin leave little doubt as to the correct diagnosis. Other diseases, such as disseminated lupus erythematosus and periarteritis nodosa, may require differentiation, but they are far less frequent than those just discussed.

Treatment

The treatment of these patients consisted of complete bed rest and the giving of 2500 to 3000 cc. of fluids daily, 8 to 10 gm. of sodium salicylate and 6 to 8 gm. of sodium bicarbonate daily, 0.033 gm. of codeine sulfate when indicated for severe joint pain and a high-calorie, high-vitamin diet. Salicylism occurred with extreme infrequency with the lower dosage. Patients with gastric distress received 4 gm. of sodium salicylate in 120 cc. of starch solution as a retention enema four times daily. In some cases 0.67 gm. of amidopyrine or 1 gm. of acetylsalicylic acid, administered four times daily instead of enemas, was well tolerated. When amidopyrine was

administered, the white-cell count was followed closely.

These dosages were usually maintained for two weeks. When the patient became asymptomatic, and the sedimentation rate normal, the dosage was reduced by a half and continued for another month. In the event of a relapse when the influence of the drug had worn off, whether with or without fever, salicylates and bed rest were resumed and were continued until the sedimentation rate had remained normal for two or more weeks. The efficacy of salicylates in the suppression of such recurrences was clearly demonstrated in these cases.

All patients were kept at complete bed rest for a mimimum period of six weeks, and it was required that the temperature, pulse, sedimentation rate and white-cell count were normal before the patient was permitted out of bed. Depending on the degree of cardiac damage, bed rest was generally maintained for four to six weeks after the electrocardiogram had become normal. The period spent out of bed was slowly increased and physical activities were graduated, special attention being devoted to the pulse.

Under such management, the joint involvement, fever and tachycardia usually subsided within three or four days, and the sedimentation rate generally returned to normal in two or three weeks. In the acutely ill patients, improvement was more protracted, seven to fourteen days elapsing before the joints, temperature and pulse became normal. With continued improvement the heart sounds returned to normal, and gallop rhythm, when present, disappeared. Systolic murmurs frequently diminished in intensity or became confined to the mitral area; in many cases they disappeared, even though formerly loud and widely transmitted.

Coburn's[3] therapeutic technic was employed in some of the acutely ill patients and in those who were refractory or showed gastric intolerance to oral therapy. Doses of 1000 to 2000 cc. of 1 per cent sodium salicylate in isotonic saline solution were administered daily by slow intravenous drip, a blood-salicylate level of at least 350 microgm. per cubic centimeter being maintained. This regime was continued until the patient was asymptomatic and afebrile, and until the sedimentation rate had dropped by about 20 per cent. When these criteria were fulfilled, intravenous treatment was replaced by oral therapy. Relief of symptoms was often effected more rapidly by this method than by others, and patients refractory to oral therapy were at times benefited. Nausea, vomiting, tinnitus and deafness, however, occurred quite often, and in 2 cases marked cerebral symptoms were noted in the form of delirium and stupor, which disappeared when salicylates were discontinued.

Sulfadiazine was given to 5 patients according to the plan generally followed in the treatment of pneumonia. No beneficial effects were noted; on the contrary, the polyarthritis became intensified and the fever remained high and continuous. No conclusion could be drawn concerning any untoward cardiac effects. In all cases, the symptoms subsided promptly when salicylates were substituted.

Penicillin was administered to 5 patients in doses of 20,000 units intramuscularly every three hours to a total of 1,000,000 units. Electrocardiograms, white-cell counts and sedimentation rates were taken daily, and the patients were kept under close observation. No beneficial effects could be attributed to this form of therapy, nor were any ill effects noted. These conclusions are in agreement with those reported by Watson, Rothbard and Swift[4] and by Foster, McEachern et al.[5] A prompt symptomatic response was obtained with salicylates in these patients.

Digitalis was employed only in patients with congestive heart failure or a persistent tachycardia of 125 or more and in those with auricular fibrillation and flutter. Aspiration of the pericardial sac was not found necessary in any patient with pericardial effusion. In 2 patients with extensive pleural effusion, thoracentesis was required for the relief of marked respiratory embarrassment.

Residual stiffness and mild aching in the joints were noted in some patients after all evidence of active rheumatic infection had disappeared; these were especially prominent during cold or damp weather. Diathermy and massage were beneficial in many of these cases. The mild aching in the feet and ankles observed on walking was improved by whirlpool baths.

Finally, although the maintenance of a high nutritional state is important, it is agreed that to attain the ultimate goal in the recovery of patients with rheumatic fever all efforts must be directed to the prevention of recurrences. Recent studies conducted by Thomas and her co-workers,[7] Coburn[8] and Holbrook[9] suggest that the incidence of recurrences may be significantly reduced by the elimination of hemolytic streptococcus infections through the prophylactic use of sulfonamide drugs. Additional well controlled studies will be necessary, however, to settle this matter beyond doubt. Furthermore, in drawing conclusions from such studies one must not lose sight of the probability that resistant strains of hemolytic streptococci may be encountered in some localities and in different epidemics. In such cases, sulfonamides are ineffective.

Summary

A composite picture of the clinical manifestations of acute rheumatic fever as observed in a series of 1000 patients in the naval service is presented.

The importance of recognizing rheumatic fever in adults is emphasized, and the difficulties in its early diagnosis are discussed.

The therapeutic effects of salicylates, sulfadiazine and penicillin are recorded.

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AINHUM*

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AINHUM, or spontaneous dactylolysis, which occurs predominately in male Negroes, has been described as a distinct disease by some authors and as a symptom by others. At the digitoplantar fold there appears a constricting ring of fibrous tissue, which deepens and finally strangulates the underlying structures, producing spontaneous amputation.

Weinstein[1] gives Messum[2] credit for the original description of the condition in 1821, but most authors give it to Clark,[3] who in 1860 described a lesion considered as a sequela to yaws in natives of the Gold Coast. The name of the disease and the first adequate description of it were published by da Silva Lima[4] in 1867, and the first pathological study was made by Wucherer.[5] Hornaday[6] in 1881 reported the first case in the United States, which occurred in North Carolina in a ten-year-old Negress.

According to Matas,[7] "ainhum" is derived from the Brazilian Negro *patois*, meaning "fissure." Da Silva Lima[4] traced it to the Nagos word meaning "sawing off." In one of the African dialects "ainhum" signifies "compression."

The greatest number of cases have been reported among the Negroes of the west coast of Africa, the West Indies and South America. Isolated cases have been reported from Europe, Russia, Istanbul and India, and about 45 cases have been seen in the United States — most of them in the southern states, a few in New York and the rest in localities scattered over the country. The case reported below is the first in New England.

A 77-year-old, unemployed Negro, a native of Barbados, West Indies, who had lived in and about Boston for the last 50 years, entered the hospital because of constriction and discoloration of the left 5th toe. He had been aware of this condition for 6 to 8 months before admission, but it had caused no symptomatic difficulty except a progressive gradual narrowing at the base. There was no history of trauma, no unusual footwear had been worn, and there had been no infection of the feet. The patient denied having had any venereal disease, by name and symptoms, diabetes or intermittent claudication. No other members of the family had had a similar condition. The diet was adequate.

Physical examination on admission revealed a well developed, well nourished, well preserved Negro, able to walk without pain or discomfort. The temperature was 98.8°F., the pulse 90, the respirations 20, and the blood pressure 170/100. The patient was mentally alert and intelligent. The skin was not discolored and was of good texture, and there were no keloid changes. The left 5th toe was purplish, warm, supple and slightly larger than the corresponding right toe. It was fissured at the digital plantar fold. Its distal portion, which was adherent at the lateral margin of the foot, was held only by a fibrous band 0.5 cm. in diameter. There was no discoloration of any of the other toes. The pulsation of the dorsalis pedis artery was faintly palpable. Sensory and vibratory sensations were physiologic, and there were no abnormal reflexes.

FIGURE 1.

The hemoglobin was 90 per cent and the white-cell count 5500, with 60 per cent neutrophils, 22 per cent lymphocytes, 8 per cent monocytes and 2 per cent eosinophils. The red cells appeared normal. The serum nonprotein nitrogen was 35 mg.

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per 100 cc., and the fasting blood sugar 95 mg. A blood Hinton test was negative. The urine was yellow and had a specific gravity of 1.020. It contained no albumin, sugar or bile. The sediment showed 1 or 2 white cells per high-power field, but no red cells or casts.

X-ray examination showed absence of the middle phalanx of the little toe and destruction of the proximal portion of the terminal phalanx, with marked osteoporosis (Fig. 1). The distal and middle portions of the proximal phalanx of the 5th toe were absent, only the base and a small, markedly narrowed fragment of the shaft remaining. There was atrophy of the bones of the foot, most marked in the toes.

There was a sharp constriction in the soft tissues of the 5th toe, which was almost completely separated from the foot. In a few days the toe became cold, dry, shriveled, firm and black and hung loosely, held only by a narrow tag of sclerotic tissue (Fig. 2).

The fibrous band was cut with scissors and the toe was painlessly removed. There was neither bleeding nor ulceration, and only a small fibrous tab of tissue remained. There was no discoloration of the skin proximal to the site of amputation. The patient remained completely asymptomatic and was discharged. Follow-up in the Out-Patient Department 2 months later showed no change in the condition of the foot.

Microscopical examination of the epidermis showed the stratum corneum to be thickened, most markedly so near the point of amputation; the stratum lucidum was not identified but the stratum granulosum was clearly defined. Nuclei were preserved in this and deeper layers. Pigment remained in the basal cell layer. The derma was composed of dense connective tissue. Within the derma and the dermal papillae, as well as within the deeper subcutaneous tissues, there were large numbers of dilated, thin-walled vessels, which were largest and most numerous just distal to the point of amputation. There was a decrease in the amount of remaining bone, which consisted of irregular trabeculae. Fat filled the trabecular spaces. No bone was found just distal to the point of amputation, where collagenous connective tissue had replaced the bone. Strands of collagenous connective tissue surrounded the centrally placed bony trabeculae. In longitudinal sections nearest the point of amputation, the tissue was composed of skin and a central core of collagenous connective tissue.

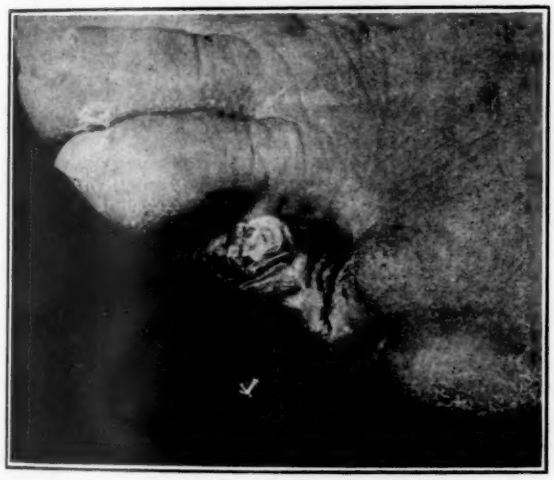

FIGURE 2.

Many theories have been advanced to explain this condition. Da Silva Lima[4] has suggested that injuries to the toes by sharp grasses produce contracting cicatrices, but the disease has been reported in Negroes who have worn shoes, and it does not occur equally in all races accustomed to going barefoot. Eyles[8] believed that the digitoplantar fold was a favorable site for irritation from foreign matter, hypertrophy of the epidermis and pressure on vasomotor nerves, resulting in the trophic phenomena. A theory that the condition is a result of leprosy, advanced by Pacha,[9] has been discarded as a result of histologic studies and bacteriologic examinations that have never shown the leprosy bacillus. Similarly, the belief that syphilis is a causal factor has been discarded. Scheube,[10] Weinstein[1] and Abbe[11] advanced the concept of ainhum as a trophoneurosis, but no nerve lesions have been found. Some writers, notably Wellman,[12] have considered infection by chiggers an etiologic factor. Davies and Hewer[13] suggested that chronic epidermophytosis might produce an excess of scar tissue and thus constriction of the toe. Constrictions resembling those of ainhum have been described in scleroderma[14] and in keratoderma.[15, 16] Bloom and Newman[17] considered the pathologic process as a mechanical one produced by a fibrotic constriction induced by some previous mechanical or infectious injury.

A few cases of this disease have been reported in white persons, notably by Arby, Debrum, Hyde–Montgomery and Castellani, according to Bloom and Newman.[17] Weinstein[1] and Doyle[18] believed that there was some familial tendency toward the disease. Ainhum rarely attacks those who have not reached adolescence, the greatest incidence being in persons between twenty and forty years of age. Weinstein,[1] however, stated that following the literature he was struck by the comparative old age of some of the patients. About 10 per cent of the cases in the United States have developed in persons between sixty and eighty years old.

Ainhum usually affects one or both of the fifth toes at the first interphalangeal articulation, either simultaneously or successively — rarely the fourth toe and less frequently the second phalanx. It generally begins as a circular depression at the internal, inferior aspect of the web of the little toe and gradually progresses, surrounding the toe, with the outer margin the last part to be involved. In most cases there is no pain at the commencement of the disease, but late in the course this symptom may be prominent. The portion of the toe distal to the locus of constriction frequently swells to a large globular segment with an intact nail. Later the phalangeal bone at the level of the constriction divides, the skin color changes, and there is loss of voluntary control. All this requires from six months to several years to develop, the course in most cases covering two to five years.

Spinzig[19] summarizes the pathological findings as follows:

> A hypertrophy of the epidermis occurs in the vicinity of the constriction. The papillae are elongated and enlarged. The arteries are thickened and engorged with blood cells, while the veins are usually empty. There is some perivascular infiltration of round cells. In the corium are usually arranged bundles of connective tissue with fat and some round-cell tissue and edema. The sweat

glands show signs of atrophy. A rarefying osteitis involves the bone with areas of destruction. Those areas are filled with connective tissue and fat and the bone is gradually replaced with fibrous tissue.

X-ray examination demonstrates the soft-tissue constrictions; there is complete or partial bony absorption of the distal phalanx and the proximal phalanx, although still present usually shows some absorption of the distal portion.

Many entities are to be considered in the differential diagnosis, but most of these are readily excluded. Leprosy mutilans is ruled out, according to Acton,[20] by the presence of anesthesia of the part, as a result of which trauma and burns produce ulcers that extend to the joints. Furthermore, all the toes are usually involved in this disease.

Morvan's disease and syringomyelia are excluded by the fact that in these diseases sensory disturbances of cold, heat and pain are lost, together with muscular power. The arms are generally affected as well.

Another condition to be considered is scleroderma. In this disease the skin is indurated, multiple digits are affected, and constitutional symptoms are frequent. The incidence is highest among females. The indurated, localized bandlike counterwork lesions may, however, offer difficulty in differentiation.

Congenital constrictions of the digits are usually not limited to the toes and are generally present from birth.

Castellani[21] believed amputation to be the best method of treatment. Da Silva Lima[4] thought that if the constriction was cut perpendicularly early it might be cured, but according to Gerwig and Warner,[22] splitting of the fibrous band is often followed by recurrence. Irgang and Alexander[23] relieved the pain in 1 case with sodium iodide. Others have tried calcium, thyroid and parathyroid, without success. Lumbar sympathectomy[24] and pavex treatment, with alternation of positive and negative pressure, have failed to influence the disease.

Summary

The first case from New England of ainhum, or spontaneous dactylolysis, is reported. The results of pathological study and the roentgenologic findings are reported, and the literature is reviewed.

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SYMPOSIUM ON MEDICAL SOCIOLOGY

FOREIGN PROGRAMS OF MEDICAL CARE AND THEIR LESSONS*

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IT IS a simple matter to state that complete medical care of the finest type is wanted for the greatest possible number of people at the least possible expense, but it is a Herculean task to translate such a need into a practical and workable plan. In the course of some sixty years, various types of medical-care programs have been tried out in a score of foreign countries. There is a wealth of experience regarding the relative merits of the basic methods of organizing and administering programs for the care of the sick. Some of the fundamental principles introduced late in the nineteenth century have proved to be sound and capable of wide application; others have been found to be inadequate, although they have not fallen into complete oblivion. In concern for tomorrow one must not forget the lessons of yesterday — and there are many lessons to be learned from both the achievements and the shortcomings of policies for organizing medical care.

Instead of describing details of some of the programs adopted abroad, I shall focus attention on the common elements in the vast number of developments that have taken place when enthusiasm crystallized into programs, and on the guiding principles of organization and administration that have emerged in the process of a piecemeal, and often haphazard, growth. I shall briefly discuss the methods of organizing professional services and facilities for medical care, the methods of organizing payment for medical care, the administrative organization of medical-care programs and the social philosophy underlying foreign developments.

* * *

In organizing professional services, the prevailing policy has been, and still is, to preserve the old-established principles of practicing medicine — those of private practice, individual practice and free choice of a physician. In a score of countries these three principles have been incorporated in social-insurance laws as well as in public-assistance statutes. They have been observed regardless of the method chosen for organization of payment for professional services. As experience accumulated, the wisdom of continuing the old policy was increasingly questioned. There was little inclination to discard the principle of private practice, but there have been some exceptions to the rule that deserve mention.

Russia, in line with her political ideology, has chosen the system of salaried medical service under government control. Private practice, although not forbidden, plays no role worth speaking of. Some hundred rural "municipalities" in certain Canadian provinces, notably Saskatchewan and Manitoba, have adopted the so-called "municipal doctor scheme," under which one or several salaried physicians are employed by the community to render service to all residents. A few months ago the Saskatchewan Government announced plans for the extension of this system throughout the province. Similar programs have been introduced in some rural areas of Australia, in particular in the Northern Territory, Queensland and Tasmania.

Whereas the principle of private practice has been maintained in the vast majority of all foreign countries, the system of individual practice has been increasingly criticized. There has been growing realization of the need to adjust medical practice to the rapid scientific progress and the profound socioeconomic changes that have taken place since the nineteenth century — the good old days when there was justification for the saying, "God cures the sick and the doctor takes the fees." It is now generally recognized that the attainment of quality, efficiency and economy of service is of prime importance in planning for the future. Two specific problems stand out as particularly pressing: the co-ordination of the work of the general practitioner and the specialist, since the latter should complement rather than supplant the former; and the integration of so-called "preventive" services and "curative" services, since these cannot be separated without injuring both.

To improve the situation, the introduction of the group practice of medicine has been increasingly recommended, primarily in the last two decades. The term "group practice" denotes a system of co-operative practice of medicine by physicians for the purpose of pooling experience and skill, facilities and equipment, technical and other auxiliary personnel and operating expenses, if not also earnings. Group practice is first of all a method to promote the scientific co-operation of the medical and allied professions for the welfare of the sick. Although it has no direct relation to the method of paying for medical care, the system gains in value if the economies it affords are passed on to the patient.

*This is the fifth of a series of nine lectures on medical sociology given weekly at Harvard Medical School during January, February and March, 1945; they were sponsored by the Department of Preventive Medicine, and were primarily intended for third-year students. These articles will temporarily replace the reports "Medical Progress."

Some of the statements in this paper are taken from the author's book *Public Medical Care* (New York: Columbia University Press, 1945). The publisher's permission to use this material is gratefully acknowledged.

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Well organized group practice conducted from a properly staffed and well equipped center, such as a clinic or a hospital, greatly benefits the patient, the health professions and the community. It provides for better and more service in a convenient way, serves to attain consistency and continuity of treatment and reduces the costs of medical care for both patients and physicians. It gives the physicians and related groups opportunities for professional improvement through consultation, research and postgraduate study, a satisfactory income, greater freedom from night calls, Sunday work and evening hours, and paid vacations. It fills a gap in the community-health program by making good medical care, both preventive and curative, available at reasonable costs.

On a limited scale, group practice has been developed in a few countries, such as Chile, France, Germany and Peru, in all instances in connection with social-insurance programs. It is interesting that in Germany group practice was abolished by the Hitler régime in line with its political ideology. Even the limited experience gained abroad clearly shows that group practice compares favorably with individual practice, since better and more service can be given at lower costs, and this tallies with the experience acquired by group clinics in this country. Significantly, recent legislative proposals in Canada and Great Britain recognize group practice and want to try it out on a larger scale. Going a step farther, the National Health and Medical Research Council of Australia has proposed the general introduction of group practice, along with the establishment of a system of so-called "consultation centers" throughout the country.

The lesson that can be learned from the development abroad is as follows. Originally, little attention was paid to the organization of professional services, and major emphasis was placed on the development of payment plans based on the insurance principle. Belatedly, it was recognized that failure to adjust the organization of professional services to modern requirements endangered the effective and economical operation of any organized program of medical care.

The organization of hospitals and clinics abroad has advanced remarkably far. The major problem was to decide on the responsibility for construction and equipment and the improvement of all the medical-care facilities necessary to meet individual requirements as well as to satisfy the community's need for adequate, humane and economical service. There are two schools of thought abroad. One group believes that all medical-care facilities ought to be established at public expense, exactly as is done with schools, highways, utilities, recreational facilities and similar services essential for the welfare of the individual as well as that of the social organism. Opponents of this policy — and there are many — insist that public policy should not deny scope and opportunity in one of the most appealing fields to the expression and practice of freely accorded individual benevolence. They do not, however, question the obligation of government to provide for certain types of facilities.

Actually one finds four distinct policies abroad. In Russia, all hospitals and clinics are owned and operated by the state. In a considerable number of countries, the great majority of all hospitals and clinics are built by local, state or national governments. Nongovernmental activities in this field are not only permitted but closely co-ordinated with those of public agencies. Nongovernmental facilities, however, must meet strict requirements as to quality, have a license to operate, and accept supervision by public authorities. Another group of countries believe that government's responsibility should be confined to provision of selected types of facilities, such as isolation, mental and tuberculosis hospitals and certain types of preventive clinics, voluntary organizations being encouraged to provide for general and allied hospitals as well as clinics of various types. Still another group of countries, including some in South America, have encouraged the construction of hospitals by social-insurance organizations.

A few examples will serve to illustrate some of these policies. In Sweden and Great Britain, all isolation hospitals are government-owned. Great Britain has about 1000 public isolation hospitals with some 40,000 beds. In Sweden, Great Britain and New Zealand, nearly all beds for mental patients are in governmental institutions, as compared with 97 per cent of such beds in this country. In Great Britain, about three fourths of all the tuberculosis beds are in public institutions, as compared with more than four fifths in the United States. In the Scandinavian countries, Austria and Germany, general hospitals are mainly public, and nongovernmental hospitals are utilized and paid by public and semipublic agencies for services rendered to designated groups. A predominantly voluntary system of general hospitals is found in France and Great Britain, although lately voluntary facilities have been losing ground. Clinics under public auspices constitute the vast majority of such facilities in a large number of countries, including the Scandinavian countries, Great Britain, Ireland, Austria, Germany and several South American countries. In Great Britain, more than 2000 school clinics and about 2500 maternal and child-health centers, or four fifths of all these centers, are maintained by public authorities.

In a score of countries, the marked change in social philosophy, expressed in the shift from private to public responsibility for the establishment of all necessary medical-care facilities, has raised intricate problems. Some groups and individuals argue that there is no longer any justification for the voluntary hospital system and hold that nongovernmental

hospitals should be abolished in favor of a system of public hospitals. Others believe that voluntary hospitals should not be prevented from operating, provided that they meet standards of adequacy and are functionally co-ordinated with governmental hospitals. The clinic problem too is being hotly debated. In the course of a haphazard development numerous types of clinics have come into existence, some organized for preventive service only, some emphasizing treatment service, some serving exclusively the needy and some admitting selected groups of self-supporting patients. The wisdom of continuing such artificial distinctions is increasingly questioned, and a new approach to the clinic problem is urged. Instead of a variety of clinics with different functions and serving different socioeconomic groups, there should be established medical centers or health centers to provide both preventive health services and care in sickness for all residents of the community. These centers should serve as the headquarters of physicians and related groups in private practice as well as of personnel employed by public and private agencies. Pertinent recommendations to this effect appear in several legislative proposals recently advanced in foreign countries.

* * *

There are two basic methods of organizing payment for professional and institutional services: taxation and insurance. When the method of taxation is used, revenues are raised primarily through taxes on property and income and to some extent through excise taxes such as sales, liquor and tobacco taxes. When the method of insurance is employed, the funds are raised in a quite different way. Insurance against the economic hazards of sickness, injury and maternity is a method of pooling risks and resources to budget and pay the cost of medical care or to compensate for loss of earnings due to disability, or to fulfill both these functions. The principle of insurance implies that many persons must band together under a single plan to spread their risks and must make small regular prepayments into a common fund to pool their resources. Thus, health insurance is organized self-help to remove or reduce the financial burden that may arise from sickness, injury or maternity. People can budget and pay for services and cash benefits when they are well and earning; they can obtain service to prevent illness and incapacity for work and receive medical care and compensation for disability when they are sick and disabled.

Both methods of financing medical care are in wide use abroad, although there are significant differences in the extent to which they are employed. Russia, in 1937, abandoned the method of financing medical care through insurance and since that time has been supporting her medical-care program out of general tax revenues. Only a few services, such as convalescent care and treatment in health resorts, are still financed through social insurance. In many other foreign countries the method of taxation is employed on a more limited scale. The policies differ greatly from country to country owing to wide variations in needs and available resources as well as in social philosophy. A few examples will serve to illustrate this point.

In Sweden, tax funds defray all but about 1.5 per cent of the expenditures for operating communicable-disease hospitals. This is an outstanding example of a policy designed to support the control of communicable disease by providing for most liberal hospitalization at public expense without regard to the economic conditions of the patient. In Ireland, there are a large number of public treatment clinics, and the policy responsible for them dates back to the early nineteenth century. These centers provide for home care as well as clinic care and serve all persons in need; the interpretation of such need is quite liberal. In a large number of countries, such as Austria, Germany, Great Britain and the Scandinavian countries, the tuberculosis-control or venereal-disease-control program, or both of them, are supported primarily out of tax funds. The eligibility standards for medical care at public expense are such as to enable the large majority of the people to receive any service they need. In some countries, there developed a multitude of special tax-supported programs with different standards of eligibility and service, all operating separately. That such a policy inevitably has patchwork results is now fully recognized. An attempt has been made in recent proposals to remedy the situation by integrating special programs into over-all programs. Nearly all foreign countries use tax funds to pay for the medical care of selected groups of persons, primarily war veterans and the recipients of public assistance. Extension of tax-supported medical care to self-supporting persons is widely regarded as unsound policy. The system of public medical care for those in need necessarily involves application of the person involved and determination of his eligibility by a so-called "means test." Under this system, the applicant and his family must have exhausted most, if not all, of their own resources before they can be accepted for a service that in the final analysis is a last resort. Charity, well intended as it is, is not what the common man wants. Restriction of service to persons in need jeopardizes preventive action. It comes too late to prevent complications, serious illness and chronic stages of sickness, and too late to permit the most economical use of the taxpayers' money. It is the considered opinion of nearly all experts abroad that the public-assistance approach to the organization of medical care is highly undesirable, and that it should be employed as little as possible.

Recognizing the inadequacy of the public-assistance approach to health security, a steadily

growing number of foreign countries have turned to programs based on the application of the insurance principle. Such plans make service available as a right, acquired by regular prepayments, and without application and a means test. Abroad, just as in this country, voluntary plans were first tried out, particularly in industry. Originally the voluntary plans paid cash to the patient so that he could pay his doctor or the hospital. The shortcomings of this method have been recognized so generally that at present nearly all nonprofit plans provide for service rather than cash allowances, whereas commercial plans usually indemnify the policyholder for medical expenses incurred. At the commencement of health insurance, plans operated for profit dominated the scene. Later, growing emphasis was placed on the development of nonprofit plans. Originally the plans were strictly limited in service, but as time went on and experience accumulated, a tendency developed to provide for more inclusive service. At that juncture the natural limitations of voluntary plans became apparent. It has been fully realized that voluntary plans can provide for selected services and reach selected economic groups, but they cannot provide for complete medical care at reasonable cost if operated on the basis of the individual practice of medicine, and they cannot reach those who need protection most. Moreover, there is the great danger that multiple, financially weak and competing organizations will develop in the same community. Vested interests are created that cannot be dislodged later, as Great Britain has experienced.

Because of the limited applicability of voluntary health insurance, some thirty countries in Europe, Asia, South America and Australia have come to adopt insurance plans required, safeguarded and subsidized by law. Mexico passed such an act three years ago. The main features of compulsory sickness insurance abroad may be summarized as follows. Certain socioeconomic groups, primarily composed of employed persons, are required to join a group plan. Persons belonging to these groups are required to make regular prepayments into a common fund, and in the case of employed persons this requirement is extended to the employers. Special legislation defines the rights and duties of the insured, the services available, the organization of professional services and hospitalization and the administrative organization of the plan, including supervision concerning adequacy and economy of service.

Often, compulsory sickness insurance is part of a comprehensive system of social insurance or social security. In many instances it provides protection against the economic risks of sickness, injury, maternity, temporary disability from sickness, injury and maternity, and death from sickness or injury, although in some countries only one or some of these hazards are covered. Protection against the economic risks of industrial accidents and certain occupational diseases is provided under special statutes, which are often incorporated in an over-all law.

The marked differences in the organization of compulsory sickness insurance abroad make it nearly impossible to give a clear picture of it in the limited space available here. All that can be done is to describe major trends of foreign developments. Such presentation may be appropriately entitled "From Bismarck to Beveridge." What Bismarck introduced in the eighties, primarily to forestall socialism, has grown to be considered a potent instrument to realize the democratic ideal of equal opportunity for everyone to obtain good medical care. Beveridge's courageous recommendations for the improvement of the British system culminate the development of sixty years of compulsory sickness insurance.

What, then, are these major trends? Originally compulsory sickness insurance covered only industrial wage earners — regardless of income — and certain groups of white-collar workers earning less than a stated amount a year. Gradually the coverage of the plans was extended by adding more groups and raising the income limit below which insurance was required. There has developed a definite trend toward including the majority of the employed persons, irrespective of the type of employment, and to apply the principle of compulsory insurance equally to industry, commerce, agriculture and domestic service. What is even more important, the family dependents of employed persons were made eligible for medical care in a steadily increasing number of countries, such as Australia, Chile, Czechoslovakia, France, Germany, Norway and New Zealand. Great Britain still excludes the family dependents but is planning to remedy this generally admitted defect in the near future. Last, but not least, voluntary enrollment in social-insurance programs is permitted in many countries. In short, whereas compulsory sickness-insurance programs originally included a minority of the people in the various countries, they now exclude a minority of the people in several countries.

The second noteworthy trend is that toward provision of complete medical care. At the beginning of compulsory sickness insurance, the medical-care provisions were meager. They still are deficient in some countries that have been slow to adjust their programs to the scientific progress of medicine. In many countries, however, the type, scope, amount and period of medical care for persons eligible for insurance service have been steadily extended. Often, the services include those of physicians, specialists as well as general practitioners, dentist's services, although with limitations, nurse-midwife services, hospitalization and the supplying of essential drugs and certain appliances. In addition, many laws authorize additional services and the exten-

sion of already established ones if sufficient funds are available.

Growing emphasis on the improvement of the quality of medical care is the third trend deserving mention. From their inception most of the foreign social-insurance schemes excluded nonmedical practitioners, and a monopoly was thus created for licensed physicians, dentists and pharmacists. Gradually the services of consultants and specialists were made available and extended, although there are still a few countries with little if any provision for such services. All the necessary diagnostic procedures and therapeutic methods were included in the programs. Excellent diagnostic laboratories and treatment centers maintained by sickness-insurance organizations in some countries testify to their strong interest in improving the quality of service. Early and frequent hospitalization has been encouraged, on the theory that such policy is not only highly valuable for the establishment of a correct diagnosis and the prevention of serious illness but also economical, since the average length of stay of the patient tends to decline as early hospitalization is promoted. In spite of all these efforts, the situation is still far from perfect, primarily because of the limitations inherent in the system of individual practice. Aware of this fact, several governments and a large number of experts abroad pay much attention to the development of group practice in connection with compulsory sickness insurance.

The fourth trend characteristic of foreign developments is that toward creation of a firm basis for the organization of and the payment for professional services. As a general rule, so-called "insurance practice" is open to all duly licensed physicians, dentists, pharmacists and members of related groups. The only condition of admission is willingness to render service according to the terms of the law and of supplementary regulations. In other words, the members of the health professions have free choice: they may participate in the program if they so desire, or they may stay out. The names of the participating physicians and other groups are placed on a list or "panel." Contrary to widespread belief in this country, private practitioners usually render service to the persons eligible for social insurance, and they attend them along with those patients who pay their own bills and those for whom a public agency foots the bill. The patient too has free choice, although there are some exceptions to the rule: free choice must not be construed as meaning unlimited free choice. No country permits indiscriminate use of the free-choice privilege. There are geographic restrictions, confining the patient's choice to physicians and allied professions residing or having offices in certain districts; and there are usually some restrictions on the selection of specialists, since a good many patients cannot be expected to know just what specialist they need. In many instances, the general practitioner sees the patient first and refers him to the proper specialist when indicated.

The methods of paying the physicians vary greatly. In many countries the capitation system is used; the participating physician receives so much per year or a shorter period for each person on his list. In some instances the flat rates paid are based on the number of patients or the cases of sickness actually treated rather than the number of persons on the list of the practitioner. In the relatively infrequent cases in which the fee-for-service system of payment is employed, a special fee schedule is established by agreement between the health professions and the organizations administering sickness insurance. The incomes of physicians and allied professions in many foreign countries come largely from payments made by compulsory sickness insurance, and this source of income is the more important the larger the number of persons eligible for service. What is changed under this system is the method of paying the doctor; what is not changed is the pattern of practicing medicine.

The funds for payment for medical care are raised primarily by regular contributions of both employers and employees, who, in many instances, share equally in the costs. These contributions are supplemented by tax subsidies from the state — usually minor ones. In certain countries, welfare departments make regular prepayments on behalf of recipients of public assistance and thus enable these patients to obtain the same service as self-supporting people.

Some of the lessons that can be learned from the development of compulsory sickness insurance abroad may now be summarized. The principle of compulsory insurance against sickness has proved to be sound, appropriate and in accord with democratic ideals. At present it is applied in some thirty countries. The existing programs, imperfect as some of them are, have benefited the patients, the participating members of the health professions and hospitals and the countries at large. Many of the shortcomings carried over from the early stages of development have been removed; some have survived and need to be eliminated. Noteworthy is the steady endeavor of all countries to make better and more provisions, the British plan for a national health service affording the best example of this trend.

Despite remarkable advances, many foreign schemes still leave considerable room for improvement. Many students of the subject criticize the policy of focusing interest on the organization of payment and neglecting action to adjust professional services to modern needs and standards. No country ever has expected compulsory sickness insurance to provide complete medical care for all the people. The reason is obvious: a program based on the application of the insurance principle can serve only

persons able to make regular prepayments, and it is hard to establish and to administer in thinly settled areas. For these reasons, all the countries having compulsory sickness-insurance programs also maintain complementary prog ams of medical care financed out of gen ral tax revenues.

* * *

The administrative organization of foreign programs of medical care is distinguished by a well known feature: multiplicity of agencies. A few significant trends may be discussed briefly. Usually, the national governments have accepted responsibility for nationwide policy-making and, to varying extents, for supervision of standards and financial participation. They share responsibility with governments at other levels. Small administrative units have been more and more discarded, since they have proved inadequate for the purpose of financing and administering medical-care programs. Instead, large units, such as counties, districts and regions, are vested with financial and administrative powers and functions. Administration of compulsory sickness-insurance schemes is generally separated from the administration of all other health services and entrusted to special statutory bodies. Thus, a state within the state has been created. The result has been overlapping, friction and waste of administrative effort on the one hand and neglect of some fields of health service on the other. The old principle of lay control of health services has been more and more abandoned in favor of professional supervision of professional matters — the physician, the dentist, the pharmacist and others each being responsible in his own field. These professional persons have authority to decide on the technical and professional aspects of medical care under social-insurance as well as other programs.

* * *

Planning for adequate medical care is more than a method of organizing the application of scientific knowledge and technical skill. It is the expression of a social philosophy. It is effective only in so far as it is sustained by a conviction of principle. The philosophy underlying modern health policy abroad rests on two cornerstones — society's need of the fit and productive person and the individual's right to health.

In essence, these ideas were expressed as far back as the end of the eighteenth century, when France issued the Declaration of the Rights of Man, and again in recent national constitutions, such as those of the Weimar Republic and the Union of Soviet Socialist Republics. New concepts have emerged, holding that the health of the people is a public concern; that sickness is more than a private misfortune; and that medical care in its widest sense is an essential human right, to be guaranteed and safeguarded in any program for personal and social security. Protection of the right to health is a fundamental function of any society aspiring to a genuine and rational economy of human resources and values. Government of the people, by the people and for the people has an obligation in this field. Nobody has expressed this better than Abraham Lincoln: "The legitimate object of government is to do for a community of people whatever they need to have done but cannot do at all, or cannot do so well for themselves, in their separate and individual capacities."

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

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CASE 32051

PRESENTATION OF CASE

A fifty-six-year-old janitor entered the hospital complaining of weakness.

Seven weeks before admission he consulted a physician because he did not feel well. He was told that he was anemic and was given liver injections. Ten days before admission he felt dizzy and faint, and at about the same time his skin became somewhat yellow. The urine was not dark, nor were the stools clay colored. At no time had the patient complained of nausea, vomiting, diarrhea or constipation. He had lost 25 pounds in weight in six months, despite a good appetite.

Physical examination revealed a pale, thin man in no acute discomfort. The skin and scleras were slightly yellow. The heart and lungs were normal. The liver edge was palpated 7 cm. below the right costal margin; it was smooth and slightly tender. The prostate was smooth, firm and symmetrically enlarged.

The temperature was 99°F., the pulse 80, and the respirations 20. The blood pressure was 100 systolic, 60 diastolic.

The red-cell count was 2,100,000, with 4.9 gm. of hemoglobin. The white-cell count was 12,000, with 82 per cent neutrophils. Many macrocytes were present, but the red cells were generally normochromic. The mean corpuscular volume was 85 cu. microns, the mean corpuscular hemoglobin 20.8 micromicrogm., and the mean corpuscular hemoglobin concentration 24.4 per cent. The urine was normal. The nonprotein nitrogen was 19 mg. per 100 cc. The total serum protein was 5.9 gm. per 100 cc., with 3.0 gm. of albumin and 2.9 gm. of globulin. The serum calcium was 7.7 mg. per 100 cc., the phosphorus 1.5 mg., and the alkaline phosphatase 27.5 Bodansky units. The serum bilirubin was 0.9 mg. per 100 cc. direct, and 1.3 mg. indirect. The serum cholesterol was 156 mg. per 100 cc. A cephalin flocculation test was ++ in twenty-four hours, and ++++ in forty-eight hours. The prothrombin time was 21 seconds (normal, 15 to 17 seconds). A bromsulfalein test showed 20 per cent retention. The gastric juice contained free hydrochloric acid. The stools varied from yellow to gray, and five out of seventeen specimens were guaiac positive.

An x-ray film of the chest was essentially negative. A gastrointestinal series revealed a normal esophagus. A small portion of the fundus of the stomach protruded through a hiatus hernia but was easily reduced. The second part of the duodenum was constantly rigid in its upper portion, with an irregular filling defect and loss of mucosal pattern along its medial wall, which contained a small central ulceration (Figs. 1 and 2). A questionable defect was present in the lower portion of the ascending part of the duodenal loop, where the mucosal pattern was preserved. A barium enema was negative.

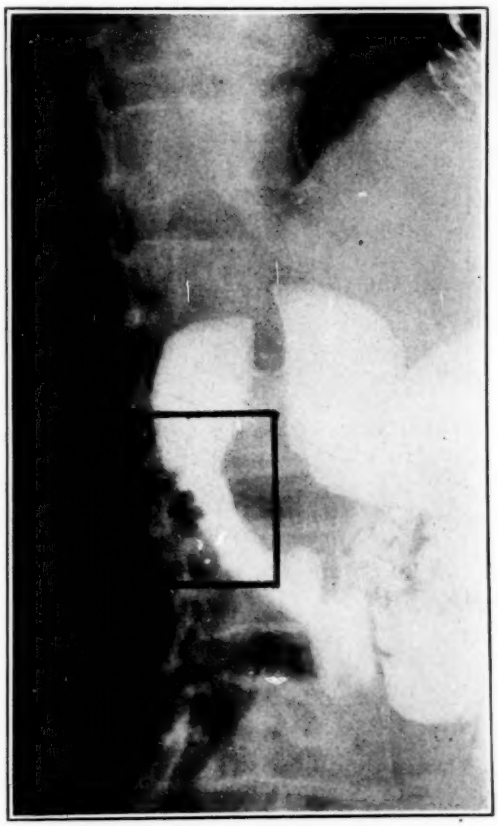

FIGURE 1. *Roentgenogram Showing Narrowed and Rigid Area of Second Portion of Duodenum.*

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. MARSHALL K. BARTLETT: May we see the x-ray films?

DR. MILFORD D. SCHULZ: The films show a normal chest and a normal colon. In the second portion of the duodenum, however, just below the duodenal bulb and along the lesser curvature, is an area of narrowing that is quite smooth and seems to be constant. It is present in a number of films. In the central portion of this defect on two films is a

little fleck that looks like barium in a punched-out defect. This shadow corresponds to the position of the ampulla of Vater.

DR. BARTLETT: Where is the other defect that was mentioned in the ascending portion?

DR. SCHULZ: It must have been a fluoroscopic observation or recorded on a film that we do not have here.

DR. BARTLETT: This man of fifty-six had been sick for seven weeks, at any rate that is when he first went to his doctor. We do not know how much longer he had had symptoms. He had been losing weight for six months but had had no symptoms referable to the gastrointestinal tract.

Physical examination adds that he was slightly jaundiced and had a palpable liver, which extended well below the costal margin. Quite a good deal of

FIGURE 2. *Enlarged View of Region of Ampulla of Vater Showing Punched-Out Defect (arrows).*

laboratory work was done — much of it because of the macrocytes seen in the smear, I presume. The various studies on the blood cells afford evidence pointing to a secondary rather than a primary anemia, although that statement is subject to correction by someone who knows more about hematology than I do. The serum bilirubin was slightly elevated, corresponding with the slight clinical jaundice. The various studies referable to the liver seem to indicate some impairment of liver function.

Certainly in a man like this we should look sharply for a malignant neoplasm somewhere. Since we are told that this man had lost 25 pounds and that his jaundice was increasing, we have to assume that it was an obstructive type of jaundice and must look for the source of the obstruction. He had had no pain, and with bleeding into the gastrointestinal tract, as shown by a positive guaiac test on repeated occasions, and a blood picture like this, one would strongly suspect a malignant tumor. I believe that we can rule out gallstones. We have x-ray evidence that suggests a lesion in or adjacent to the duodenum that had ulcerated through into the duodenum. So as I see it, my function is to make a choice between a lesion of the ampulla or in the duodenum proper and a lesion in the head of the pancreas that had ulcerated into the duodenal wall. I do not know any way to make a sure decision. Since Dr. Schulz has suggested that the lesion was in the region of the ampulla, I will put that as my first choice, with carcinoma of the head of the pancreas as the second.

DR. TRACY B. MALLORY: You are assuming that, if the lesion was in the ampulla, it was malignant?

DR. BARTLETT: Yes.

DR. JAMES H. TOWNSEND: Was no attempt made to visualize the gall bladder?

DR. MALLORY: A peritoneoscopy was done preoperatively. It showed a smooth, enlarged, bile-stained liver and a slightly dilated gall bladder. No fluid was found in the abdominal cavity, and a liver biopsy showed only bile stasis.

CLINICAL DIAGNOSIS

Carcinoma of head of pancreas.

DR. BARTLETT'S DIAGNOSIS

Carcinoma of ampulla of Vater.

ANATOMICAL DIAGNOSIS

Adenocarcinoma of ampulla of Vater.

PATHOLOGICAL DISCUSSION

DR. MALLORY: Dr. Scannell, I believe that you operated on this man. What were your findings?

DR. JOHN G. SCANNELL: This man was operated on in two stages. The first consisted of drainage of the gall bladder and the establishment of a feeding jejunostomy. At that time a mass was palpated in the head of the pancreas, but its size could not be accurately determined. In two weeks we re-explored, and a small freely movable tumor was demonstrated in the head of the pancreas in the region of the ampulla; this mass was fairly readily resected. The common duct, I might add, which was not well visualized at the first exploration, was found to be tremendously dilated; the gall bladder was dilated, but the edema had completely disappeared.

DR. MALLORY: At the second operation, considerable portions of the duodenum and head of the pancreas were resected. The tumor appeared to be limited to the ampulla. It involved the full thickness of the duodenal wall, but so far as we could make out it did not penetrate the pancreas. There were no obvious lymph nodes. The area of resection appeared to be entirely adequate. I do not believe that the prognosis is excellent, but it is not impossible that a cure has been effected.

DR. BARTLETT: What type of tumor was it?

DR. MALLORY: An adenocarcinoma, fairly well differentiated. It is worth remembering in considering operation on such a patient that benign polyps of the ampulla are not extremely rare. Exploration, at least, is certainly indicated.

DR. BARTLETT: Was the duodenum ulcerated?

DR. MALLORY: There was slight ulceration of the surface of the tumor. No gross crater was evident.

DR. BARTLETT: What was done with the bile duct? Was the surgery complicated?

DR. LELAND S. MCKITTRICK: I like the way that Dr. Scannell passed over that.

DR. SCANNELL: A loop of jejunum was selected about 45 cm. below the ligament of Treitz; it was transected, and the proximal end was implanted into the side of the distal portion. An end-to-end anastomosis was then effected, after the manner of Dr. Allen,* between the cut ends of the common bile duct and the distal jejunum over a catheter, which was led out through the wall of the jejunum and through the abdominal wall, to be removed in about three weeks. The cut ends of the pancreas and of the stomach were then implanted into the side of this loop.

DR. MALLORY: Did the patient develop a pancreatic fistula?

DR. SCANNELL: On the tenth postoperative day he drained considerable material from the upper end of the wound, but this has since decreased to nil. From the character of the material I should judge that it was from a high jejunal or pancreatic fistula. We were unable to demonstrate the pancreatic duct at the time of exploration and therefore implanted the cut end of the pancreas into the subserosa of the jejunum.

CASE 32052

PRESENTATION OF CASE

A sixty-five-year-old woman entered the hospital complaining of abdominal pain.

For two years before admission she had had an intermittent dull ache in the right upper quadrant. The pain occasionally radiated to the back and was not associated with nausea, vomiting or anorexia. It had no relation to the ingestion of food. It lasted for about twenty-four hours, subsided and then recurred in a few days. At times she also had dull aching pain across the lower abdomen, not related to the distress in the right upper quadrant. The latter complaint was made worse by constipation but was not relieved by a bowel movement. An intermittent midepigastric distress had also been present for a year and a half. Five months before admission she was seen at another hospital, where she was told that she had a growth in the stomach. She was given a chalky milklike fluid, which she took for three months and which seemed to relieve the epigastric pain and belching.

She had had rheumatic fever at twenty-five years of age, with no residual heart disease but with persistent joint pains. She had been known to have hypertension for fifteen years before admission and had been treated for syphilis for ten years, although she denied a history of venereal disease. Three years before admission she suddenly lost vision in the right eye, but it slowly returned. She had had three miscarriages.

The physical examination revealed a well developed and nourished woman in no acute discomfort. The pupils reacted normally to light and accommodation. The border of the heart was 11 cm. to the left of the midline in the fifth interspace. A systolic murmur was heard over the aortic area. The lungs and abdomen were negative. Neurologic examination was negative.

The temperature was 97°F., the pulse 70, and the respirations 15. The blood pressure was 230 systolic, 110 diastolic.

The red-cell count was 4,200,000, with 12 gm. of hemoglobin. The urine was normal. The nonprotein nitrogen was 15 mg. per 100 cc., and the total protein 5.9 gm. The chloride was 90 milliequiv. per liter. A blood Hinton test was positive. Lumbar puncture yielded a clear fluid, with normal dynamics; the fluid contained 350 red cells per cubic millimeter. The total protein was 34 mg. per 100 cc., and the gold-sol curve 0001100000.

A gastrointestinal series showed a normal esophagus and a small hiatus hernia. There was some narrowing, as well as absent peristalsis, of the prepyloric region of the stomach (Fig. 1). No peristaltic waves were seen to pass through the immediate prepyloric region. It was not possible to palpate this area. There was an apparent crater about 8 mm. in diameter somewhat toward the margin of the lesser curvature. The duodenal cap was small but not deformed. A barium enema showed numerous diverticulums in the sigmoid. On gastroscopy the instrument passed readily. When first examined the angulus was tightly and smoothly closed, without any spasm or ropelike contraction. With air inflation the angulus opened and presented a normal appearance. Slow peristaltic waves were seen to pass over the proximal antrum, which appeared somewhat granular but was otherwise normal. The distal antrum and the pylorus were not visible. The body of the stomach appeared normal throughout.

An operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. DANIEL S. ELLIS: I should like to call attention to the fact that this woman's pain was not associated with nausea, vomiting or anorexia. The history does not state whether she had these symptoms at the time of admission, yet I am forced

*Allen, A. W. Method of re-establishing continuity between bile ducts and gastrointestinal tracts. *Ann. Surg.* 121:412-424, 1945.

to conclude from the chemical values given in the laboratory data that the patient had been vomiting. I do not know how else to explain the low chloride and the high carbon dioxide in the absence of renal disease.

I assume that the red cells in the spinal fluid were due to the trauma of the tap. We are not told the result of the spinal-fluid Wassermann test. Perhaps the test was not done. In the absence of that information I am going to assume that the spinal fluid was normal.

From the available history there is one thing that I am sure of, namely, that an operation was a prerequisite of diagnosis.

May we see the x-ray films?

DR. MILFORD D. SCHULZ: This film is put up simply to show that the colon and gall bladder were normal. This next film shows an area of irregularity in the antrum and in the prepyloric region of the stomach. This last film, I believe, shows best what was thought to have been an ulcer crater. There is apparently some rigidity about it along the lesser curvature side of the antrum and in the prepyloric region. The duodenal bulb is quite normal.

DR. ELLIS: Can you see a mass in the prepyloric area?

DR. SCHULZ: No.

DR. ELLIS: What about the mucosal markings?

DR. SCHULZ: They are not normal. Some markings look like mucosal folds, but I wonder if they do not represent just a puckered and swollen stomach wall. Certainly, it is not a normal mucosal pattern.

DR. ELLIS: Is that the only film of the gall bladder?

DR. SCHULZ: No, but it is a representative one.

DR. ELLIS: May we see a film of the chest?

DR. SCHULZ: None are available.

DR. ELLIS: We have, then, the story of a patient, sixty-five years of age, who we know had hypertension of some degree, with cardiac enlargement,

FIGURE 1. *Roentgenogram of Stomach following Barium Meal.*

diverticulums of the sigmoid, which could account for the discomfort low in the abdomen, and a small hiatus hernia, which may or may not have contributed to her symptoms in the past. In addition, the factor of primary importance, — the one that apparently resulted in her hospitalization, — was a lesion of the stomach and, as I see it, my problem is to say what that lesion was.

It seems to me that the differential diagnosis is clear and lies between one of three things: carcinoma of the stomach, benign peptic ulcer and syphilis of the stomach. The latter diagnosis has rarely been proved. When it occurs it may resemble ulcer but is likelier to resemble carcinoma. It is usually associated with weight loss, vomiting, anorexia, anemia and achlorhydria. The criteria for a clinical diagnosis of gastric syphilis are the proper age group (usually under forty), collateral evidence of syphilis, x-ray evidence of a tubular prepyloric obstruction, improvement under antisyphilitic therapy and a lesion found at operation with the microscopic characteristics of syphilis.

The symptoms and x-ray evidence, as well as the positive Hinton test, are the positive indications for such a diagnosis in this case. This patient, however, was in an older age group, and there is no evidence that ten years of antisyphilitic therapy had helped her stomach trouble.

On the basis of the patient's age and the location of the lesion the chances that this was a benign ulcer are remote. A benign ulcer, however, may have enough inflammatory reaction around it to give an x-ray picture such as the one we have just seen, and the fact that this patient was not anemic and was reported to be in a good state of nourishment also favors a diagnosis of a benign lesion, especially in the light of the prolonged history of symptoms and the proof of a gastric lesion of at least five months' duration.

Finally we have to consider malignant disease of the stomach. This lesion is located in the prepyloric region, where 70 per cent of all gastric cancer is found. Twenty-five per cent of the remaining gastric tumors occur on the lesser curvature, and in this case there was an ulceration on the lesser curvature. To know whether this patient had achlorhydria and exactly how much weight she had lost would be helpful. As I said in the beginning, the one thing that I am sure of is that the only way an accurate diagnosis could have been made in this case was by operation, and even then, microscopic examination of the specimen may have been necessary.

In conclusion I shall say that I do not believe this woman had gastric syphilis or that she had a benign peptic ulcer. My final diagnosis is malignant disease of the stomach, probably an adenocarcinoma, with partial pyloric obstruction; she also had essential hypertension and hypertensive heart disease, diverticulums of the sigmoid, latent syphilis and a hiatus hernia, the last being an incidental finding and not contributing to her symptoms.

Dr. Tracy B. Mallory: Are there any comments or alternative diagnoses?

Dr. James A. Halsted: Chronic gastritis might give this picture.

Dr. Mallory: Has the roentgenologist anything to say about that?

Dr. Schulz: There is no evidence of fluid, and the gastric rugae are not greatly swollen.

Dr. Mallory: Dr. Scannell, will you tell us about the gross findings at operation?

Dr. John G. Scannell: We were intrigued by the prepyloric region at operation. The stomach was freely movable, with no gross retroperitoneal disease. There was an area of induration in the prepyloric area that involved the whole circumference of the stomach, not being limited to the lesser curvature. We thought it probably was benign disease, but we could not tell what it was. There were no enlarged lymph nodes, but since we were doing the operation for potentially malignant disease, we removed the omentum and secured the left gastric artery at its source. On opening the resected portion of the stomach, we were still at a loss to explain the nature of the disease. There were shallow ulcerations in the mucosa, and the wall of the stomach was indurated but not adherent to surrounding structures.

Dr. Francis M. Rackemann: Was there any disturbance of the blood supply?

Dr. Scannell: No obvious disturbance.

Clinical Diagnosis

Carcinoma of stomach.

Dr. Ellis's Diagnosis

Carcinoma of stomach.

Anatomical Diagnosis

Lymphoblastic lymphoma of stomach.

Pathological Discussion

Dr. Mallory: The pathologist was likewise unable to decide from examination of the gross specimen whether the lesion was benign or malignant, although the latter seemed a little more probable. The diagnosis had to wait for microscopic examination, which showed a malignant infiltrative tumor that proved to be a lymphoma and not a carcinoma.

Following resection, the patient was started on x-ray therapy, and she is still in the hospital undergoing treatment. The outlook in these cases is not too bad. With a combination of resection and radiation, "cures" of five or more years sometimes occur.

Dr. Benjamin Castleman: Were the lymph nodes involved?

Dr. Mallory: No large nodes were found.

Dr. James H. Townsend: Do lymphomas usually ulcerate?

Dr. Mallory: They may or may not. Sometimes they produce extremely large ulcerations.

Dr. Fletcher H. Colby: That means that a lymphoma may be localized?

Dr. Mallory: In the gastrointestinal tract it is quite frequent to find localization in the wall of the viscus, with the immediate nodes entirely negative. Even when the nodes are enlarged there is frequently no microscopic evidence of infiltration.

Dr. Schulz: In the absence of involvement of the regional nodes or of remote disease, I wonder about the need for x-ray therapy with the lesion presumably so completely removed.

Dr. Mallory: We have a few long cures on record from surgery alone, but there are not enough of these cases to compare with those receiving the combined treatment for statistical analysis.

Dr. Frederick Kranes: What type of lymphoma was this?

Dr. Mallory: We classified it as a lymphoblastic lymphoma, although the cells were not extremely immature.

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The JOURNAL does not hold itself responsible for statements made by any contributor.

COMMUNICATIONS should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

NATIONAL SOCIAL HYGIENE DAY

FEBRUARY 6 is National Social Hygiene Day, the tenth annual event of its kind on a national basis. It had its beginning as a series of meetings held across the country on the day of the annual meeting of the American Social Hygiene Association, being an alternate for members unable to travel to the meeting, but in 1937 it was given formal recognition by designating the day by this name. It has come to be a day on which pledges are renewed to the achievement of the high standards set by the founders of the Association. These founders had as their major objective the protection of the family and its members from the perils to health, happiness and home that result from venereal disease and prostitution. The full attainment of these aims is chiefly concerned with an attempt to guide schoolteachers, religious leaders and parents, as well as physicians, in the furnishing of wise counsel concerning the sex problems of the younger generation. The achievement of its objective is a co-operative undertaking requiring the energies of local and national associations and groups of many types, such as health departments, social agencies, physicians, nurses, educators, church leaders and Army and Navy venereal-disease control centers, for its successful completion.

Great advances have been made in these ten years in the fields of diagnosis and treatment of syphilis and gonorrhea. The dramatic success of penicillin as a therapeutic agent is still unfolding, but the final estimate of its value, especially in syphilis, can only be measured by medical experience with the drug over a period of years. In the meantime the early diagnosis of syphilis and gonorrhea is essential. The campaign for the prevention of these diseases must proceed with increased vigor. Education, that is, education of the patient, the family and the public at large, is the essential feature of any preventive program directed at these diseases. The publication of a recent study by the Advisory Committee on Public Education for the Prevention of Venereal Disease of the United States Public Health Service* occurred at an opportune moment. Among the recommendations of this committee three items should be emphasized: first, that venereal-disease education is a primary responsibility of official health agencies and should be conducted by them on an intensive and a sustained basis; second, that this education should be coordinated with other health-education programs; and third, that there should be a considerable expansion of facilities for training health-department personnel who are to engage in these activities.

Participation of the physician in this campaign for the protection of the individual and the family obviously demands early diagnosis, adequate treatment and the routine reporting of cases of venereal disease, as directed by the laws of his state. As a citizen as well as a physician he has a large obligation, by reason of his medical knowledge, to participate to the fullest extent in organized activities

*Report of United States Public Health Service Advisory Committee on Public Education for the Prevention of Venereal Diseases (July 18, 1945). *J. Ven. Dis. Inform.* 26:256-263, 1945.

for the education of the public and the prevention of these infections, in accordance with the plans developed by public-health departments and associations dedicated to this cause.

"ELSE WHENCE THIS PLEASING HOPE"

MUCH has been written on the medical and surgical care of the patient, volumes have been published on the treatment of the mentally ill, but little has been said and even less has been written on the psychologic aspects of patients who are gravely ill or who are suffering from a fatal disease. An excellent approach to this subject has come from the pen of a layman, Ben Ames Williams,* who, to his discomfiture but to the advantage of the public, has contrived from time to time to become ill. He has been able, therefore, "To see ourselves as others see us" and to point out to us doctors the psychologic pitfalls that lie before us, but in addition he has given some very constructive and valuable advice concerning their avoidance. To those who have not read his article, we recommend it; to those who have, we suggest that they read it again.

In last week's issue of the *Journal* appeared the concluding paper of a series of articles on Hodgkin's disease, and therein are contained a few words of advice concerning the psychologic care of patients with a disease that is almost always but not invariably fatal. Of the last six words of the previous sentence the most important, far and away, are "but not invariably": for in these words lie one of the subtle secrets of the care of the patient.

What have we to offer to patients with this condition or allied ones? X-ray therapy, certainly; transfusions, probably; radical surgical intervention, rarely. Can we offer the hope of a true cure? Yes, but only once in hundreds of cases. Yet, who can predict in the individual case, granting that it be early, whether or not a cure will result. Herein lies the second secret.

Above all we can offer hope. That we can and must give in order that the patient's days, whether they be short or long, be ever full of hope, not despair. Nearly three years ago a young soldier who had been through the Kasserine Pass both ways was suddenly invalided home for reasons quite unknown to him, because he felt perfectly well. In the States he was with equal abruptness and greater bluntness told "the truth" — that he had leukemia, that he would live but a few months and that nothing could be done. Shortly after he was boarded out with a Certificate of Disability Discharge, he consulted a civilian doctor. From him he received hope, and the tense, distraught, despairing, frightened soldier became a happy, hopeful young man. No diagnosis was mentioned. Rather it was stressed that much could and would be done and that he could reasonably look forward to an active and useful life. Indeed, his illness was so minimized that the patient came, quite surely, to believe that he did not have leukemia. Two years later he rather shyly slipped into his physician's hand a newspaper clipping about a new cure for leukemia. "I just thought I would ask if there is anything in that, doctor." "No, I'm afraid there isn't." No more was said. The boy had grown to know the truth, but its impact was gone because of the insidiousness of its realization. Today, three years and more after the battle of the Kasserine Pass, that boy is alive and happy and active. The diagnosis, if the real truth be known, is not entirely clear; but the facts are as stated. Hope we can give; the patient's burdens we can, to a great extent, take unto ourselves.

MASSACHUSETTS MEDICAL SOCIETY
POSTWAR LOAN FUND

The Postwar Loan Fund has been set up, and all discharged medical officers who were members of the Massachusetts Medical Society in good standing at the time of their entry into the service may apply for loans from this fund. For further information apply to:

George L. Schadt, *Chairman*
Postwar Loan Fund
8 Fenway
Boston 15, Massachusetts

*Williams, B. A. The Greeks had a word for it. *New Eng. J. Med.* 233:427-432, 1945.

But it is not always the patient who must be treated with gentleness: it is not always the patient in whom we must, at all costs, inspire hope. He may be quite oblivious of the truth while his friends or relatives may be distracted almost beyond control. Then we must turn our attention to these good people, if only to protect the patient.

If we are to give hope we must learn the gentle art of evasion — not lying, mind you, but evasion. Recently an extremely astute man with some knowledge of medicine and indeed of his own disease, aplastic anemia, asked his physician point blank: "Does it not follow, doctor, because my general health and sense of well being have greatly improved in the past two weeks and because the ulcerations in my mouth have entirely cleared, that my anemia will similarly improve?" It did not follow in the slightest. But cannot we reply without hesitation — to hesitate is to fail — that we hope that such will be the case and pass rapidly on to less contentious matters before the patient recognizes that we have said "hope" not "will"? That patient died ten days later at home, having in the meantime spent three days with friends in New York City. He had no wish to hurry home. Was he not filled with hope?

NOTICES

ANNOUNCEMENTS

Dr. Sawyer Foster is resuming the practice of internal medicine at 144 Commonwealth Avenue, Boston.

Dr. George A. Marks, having returned from military service, announces the reopening of an office at 1101 Beacon Street, Brookline, for the practice of surgery.

Dr. Edward T. Moses, having returned from active service with the United States Army, has opened his office at 632 Main Street, Malden, for the practice of neuropsychiatry.

Dr. Jules H. Shaw announces his return from military service and the opening of offices at 510 Commonwealth Avenue, Boston, for the practice of ophthalmology.

Dr. Howard B. Sprague, having returned from active duty in the United States Navy, is resuming the practice of cardiology at 270 Commonwealth Avenue, Boston.

Dr. Ralph Volk, having completed active service with the United States Navy, announces his return to the practice of medicine at 1411 Beacon Street, Brookline.

GREATER BOSTON MEDICAL SOCIETY

A meeting of the Greater Boston Medical Society will be held in the auditorium of the Beth Israel Hospital on Tuesday, February 19, at 8:15 p.m. Dr. Edwin J. Cohn and Dr. Charles A. Janeway will speak on the subject "The Chemical Separation and the Clinical Appraisal of the Components of the Blood."

TUFTS ALPHA OMEGA ALPHA

The Tufts chapter of the Alpha Omega Alpha will meet in the Auditorium of the Beth Israel Hospital, Boston, on Wednesday, February 27, at 8:30 p.m. Dr. George R. Minot will speak on the subject "The Art of Medicine."

PRIZE CONTEST

The American Association of Obstetricians, Gynecologists and Abdominal Surgeons Foundation has recently announced that the annual prize contest will be conducted again this year. Requests for detailed information should be addressed to the secretary, Dr. James R. Bloss, 418 Eleventh Street, Huntington 1, West Virginia.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Thursday, February 7

Friday, February 8

*9:00–10:00 a.m. Medical clinic. Isolation Amphitheater, Children's Hospital.

*9:00–10:00 a.m. Physiologic Evaluation of Quartermaster Clothing and Equipment. Colonel John H. Talbot. Joseph H. Pratt Diagnostic Hospital.

*10:00 a.m.–12:00 m. Medical staff rounds. Peter Bent Brigham Hospital.

10:50 a.m. Rationale of Pharmacology in Dermatology. Professor L. M. Ohmart. (Postgraduate clinic in dermatology and syphilology.) Amphitheater, Dowling Building, Boston City Hospital.

12:00 m.–1:00 p.m. Clinicopathological conference (Boston Floating Hospital). Joseph H. Pratt Diagnostic Hospital.

Monday, February 11

*12:00 m.–1:00 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

Tuesday, February 12

*9:00–10:00 a.m. Medical clinic. Infants' Hospital.

*12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

8:00 p.m. Harvard Medical Society. Peter Bent Brigham Hospital.

Wednesday, February 13

*9:00–10:00 a.m. The Treatment of Laennec Cirrhosis. Dr. Roy C. Crosby. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. Clinicopathological conference. Children's Hospital.

*12:00 m.–1:00 p.m. Clinicopathological conference. Cambridge Hospital.

*7:15 p.m. Graduate seminar in pediatrics. Children's Medical Service, Amphitheater 3A, Massachusetts General Hospital.

*Open to the medical profession.

January 7–April 22, 1946. Metropolitan State Hospital. Eleventh postgraduate seminar in neurology and psychiatry. Page 314, issue of September 6.

February 2. American Board of Obstetrics and Gynecology. Page 514, issue of October 25.

February 4–March 29. Health Education Institute. Page 746, issue of December 13.

February 7. New England Hospital for Women and Children. Page 136, issue of January 24.

February 9. New England Dermatological Society. Page xix, issue of January 17.

February 12. Harvard Medical Society. Peter Bent Brigham Hospital. 8:00 p.m.

February 13. Massachusetts Medico-Legal Society. Page xix, issue of January 17.

February 14. Diagnostic and Therapeutic Suggestions in Cardiovascular Disease. Dr. John Sproull. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

February 19. Greater Boston Medical Society. Notice above.

February 20. Tufts Medical Alumni Lecture. Page xix, issue of January 17.

February 27. Tufts Alpha Omega Alpha. Notice above.

May 13–17. American College of Physicians. Page 798, issue of December 20.

District Medical Society

WORCESTER

February 13. Worcester State Hospital.

March 13. Worcester Memorial Hospital.

April 10. Hahnemann Hospital.

May 8. Annual meeting.